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REVIEWS

TYPHOID AND PARATYPHOID FEVERS

Aetiology. In an article on typhoid, paratyphoid, and dysentery carriers among returning overseas troops Schorer states that in only two of a thousand individuals were any of the usual pathogenic intestinal Gram-negative bacilli present. These men were found to be carrying dysentery bacilli of the Hiss-Russel-Y and Flexner types respectively. No typhoid or paratyphoid bacilli were isolated. Therefore, only 0·2 per cent. of all the men examined were carriers. These results show that such infections as had occurred in the American Expeditionary Force during the autumn and early winter of 1918 had remained limited, and gave rise to no aftermath of carriers. The number of clinical cases of similar infections among returning troops were as follows: of 50,747 men passing through the hospitals of the Port of Embarkation during March, April, and May, 1919 six had typhoid fever and one dysentery of the Hiss-Russel-Y type. There were no cases of paratyphoid.

In 1916 Minet was able to isolate in four cases the paratyphoid A bacillus, in two the paratyphoid B bacillus, and in one Gaertner's bacillus from the sputum of enteric cases. Since then he has frequently been able to confirm his original observations which show that the different varieties of paratyphoid bacilli may be localized in the respiratory system and be discharged in the sputum. Clinically this localization may give rise to symptoms of varying intensity, such as simple bronchitis, acute pulmonary congestion, and congestion of the apex simulating tuberculosis. The practical importance of Minet's observations is that they reveal a new mode of contagion for paratyphoid—contagion by the sputum—and a new kind of paratyphoid carrier—a carrier of pulmonary organisms.

As the result of her experiments Gillot found that the white mouse can resist an intraperitoneal infection with a virulent culture of typhoid bacilli after prophylactic injection of antityphoid vaccine or injections of human serum. The power of resistance conferred by the latter is earlier, stronger and more lasting. Thus a mouse can resist 2 c.c. of a virulent culture when it has been given progressive doses of a vaccine for 73 days, or when it has had 1 c.c. of human serum injected at the same time as the culture. The maximum preventive action is that of normal serum from a young individual. Gillot emphasizes the paradoxical fact which is in opposition to the results obtained by previous writers that human antityphoid serum, i. e. serum of individuals who are or have been suffering from typhoid fever or have been inoculated with antityphoid vaccine, is absolutely inert in circumstances where normal human serum confers on the white mouse the most powerful immunity against typhoid infection when the serum and virulent culture are injected simultaneously.

Laboratory infection. Hirschbruch and Forthmann record a case of a female laboratory assistant who accidentally infected herself while sucking up a culture of typhoid bacilli in a pipette. She had been inoculated against typhoid three years previously. Immediately after getting the culture into her mouth she washed it out with absolute alcohol, some of which she swallowed. Symptoms of typhoid developed exactly 13¼ days later. The writers allude to Kisskalt who, as the result of a questionnaire, published a collection of 57 cases of laboratory infections with typhoid, of which half and perhaps more were due to the use of the pipette. It was found that recent cultures often gave rise to mild attacks, whereas cultures which had been grown on artificial media for years, as in the present writers' case, often caused a severe illness. Seven of Kisskalt's cases had been inoculated against typhoid 4¼ years before contracting the disease.

Other possibilities of infection in laboratories are the accidental breaking of culture tubes and spilling them on the clothes with subsequent infection of the mouth, external contamination of vessels containing specimens of stools, and soiling the fingers in handling plate cultures, the cover of which is broken. Lastly, laboratory tables may be contaminated during the preparation of a hanging drop culture or a preparation of Widal's test. When infection has taken place it is advisable to wash out the mouth with a disinfectant solution and take a powder three times a day containing tannoform 1 gm. and calomel 0·3 gm. The writers doubt the value of inoculating laboratory workers as the protection conferred lasts only a short time, and the inoculation would have to be repeated extremely frequently. The use of typhoid vaccine after actual laboratory infection is also doubtful, as the disease usually develops in such cases after an incubation period of 12 days, whereas the vaccine does not confer complete protection until 21 days.

Symptomatology. Heiman and Crespin and Athias respectively have recently reported cases of **typhoid fever in infants** who had been suckled by mothers ill with the disease. In Heiman's case typhoid bacilli were found in the milk. The infant, which was aged 8 months, had a severe attack, though the issue of the case is not recorded. Heiman had been unable to find any similar case on record, but alludes to a case reported by Lawrence (*Boston M.* and *S. J.*, 1909, **151,** 153) in which, though typhoid bacilli were found in the milk of a nursing mother suffering from typhoid, the child escaped infection. In the case reported by Crespin and Athias the infant, which was aged 3 months, had to be weaned owing to the severity of the mother's attack of typhoid. Though in the course of 10 days it nearly lost a kilo in weight, its general condition appeared to be good, when one morning it was found dead in bed. The autopsy showed enlargement of Peyer's patches, mesenteric glands and spleen and a haematoma of the left suprarenal. The case illustrates the frequently latent course of typhoid fever in the infant, and is an example of the close association between suprarenal haemorrhage and sudden death.

Typhoid fever in old age. Gioseffi reports four cases of typhoid fever in persons over 70, which were remarkable for the mildness of their course. A man aged 82 fell ill 17 days after his daughter with diffuse bronchitis, enlargement of the spleen, a temperature of 100·4 and a positive Widal's reaction. Two patients, aged 72 and 74, respectively, had a similar attack. A woman aged 80 fell ill with a subfebrile temperature, drowsiness, hypochondria, and dysuria. Widal's reaction was positive 1:500. Recovery took place.

At a recent meeting of the Hamburg Medical Club Fraenkel showed specimens from two cases of **rupture of the spleen** in typhoid in men aged 30 and 36, respectively. In the first case the diagnosis was made by finding typhoid bacilli in the blood, and in the second, which was moribund on admission to hospital, by the character of the stools. In both cases at the autopsy large quantities of clot and fluid blood were found in the abdominal cavity, and the capsule of the spleen showed a tear, the edges of which, and adjacent parts of the surface, were covered with a thick layer of clot. On microscopical examination an unusually large number of groups of typhoid bacilli was found in the spleen, as well as necrotic foci in the spleen pulp, some of which were lying near the surface in the inner layer of the capsule. The intestine in both cases showed swelling of the lymphoid tissue which in one case was undergoing sloughing in places. In one case the lesions were confined to the lower part of the ileum, and in the other involved the whole of the ileum and solitary follicles in the caecum. These were the only two examples of rupture of the spleen which Fraenkel had seen in 426 autopsies on typhoid fever cases at the Eppendorf Hospital and on an equally large number at St. George's Hospital, Hamburg. As regards the clinical symptoms, Fraenkel remarked that only a probable diagnosis was possible, the occurrence of acute anaemia without previous intestinal haemorrhage being suggestive of rupture of the spleen.

A case of isolated **post-typhoid paralysis** of the crico-arytenoideus posticus, which developed seven days after the temperature had become normal, is recorded by Romanofski. At first no inflammation or even catarrh of the larynx was seen on laryngoscopy, but after the paralysis had lasted about seven weeks acute laryngitis occurred necessitating tracheotomy and the wearing of a permanent tracheotomy tube. The writer thinks it probable that there was a degeneration of the crico-arytenoideus posticus, for it was very unlikely that only those fibres of the recurrent laryngeal which supplied the abductors of the glottis should be affected, and that the rest of the nerve should be intact. In favour of muscle degeneration was also the fact that the patient was much debilitated although the attack of typhoid had not been very severe, and it is probable that the supine decubitus which caused a pressure of the larynx against the vertebral column created a *locus minoris resistentiae* in the muscle.

Nicaud reports a fatal case of typhoid **meningitis** in a man aged 25 which occurred in 1917 a year after three injections of T. A. B. vaccine. In 1914 he had been inoculated with a simple typhoid vaccine. The typhoid bacillus was cultivated from the turbid cerebrospinal fluid during life, and the necropsy showed early lesions in the small intestine and extensive suppurative meningitis.

Löwy reports a fatal case of **pleuro-pneumo typhoid** in a man aged 64. A pure culture of typhoid bacilli was obtained from a serous pleural effusion which showed a lymphocytosis. A few days before death the patient developed haematuria and progressive anaemia. The necropsy showed a recent haemorrhagic nephritis and remains of pleurisy over the right lower lobe. Bacteriological examination of the bile and spleen was negative, and no lesions were found in the intestine or mesenteric lymph glands (cf. *Medical Science*, 1919, **1**, 26).

Abram and Glynn report two cases of paratyphoid B infection of the pleura, one being an example of sero-fibrinous pleurisy in a man aged 38, and the other one of empyema in a woman aged 24. In the first case the patient had had some diarrhoea with slight pyrexia, and typhoid had been suspected, but the stools were not examined. In the second case the symptoms were those of influenza, and the faeces were examined with a negative result. A brief account of other cases reported in the literature is given.

Hage states that a few cases of **paratyphoid infection of the gall-bladder** with calculus formation and without any coexistent intestinal disease have been recorded. Lorey, in one case of the kind, found paratyphoid B bacilli, and Blumenthal and Springer each reported a case due to the paratyphoid A bacillus. Hage himself relates a case of cholecystitis due to paratyphoid B infection in a man aged 41 who had no previous symptoms of paratyphoid involvement of the intestine. The presence of calculi in the gall-bladder could not be determined as operation was refused, and no stones were found in the stools. The case shows the necessity of making a serological and bacteriological examination for paratyphoid bacilli in all cases of cholecystitis, even when there are no obvious signs of intestinal disease.

According to Ollivier, who records an illustrative case in a woman aged 20, an acute peritoneal syndrome called 'false perforation' (Rochard) may occur in paratyphoid B as in typhoid fever. It is almost always impossible to diagnose between a true and a false perforation, and an exploratory operation should be carried out at once. On laparotomy the following appearances may be found: 1. No lesion at all. 2. A few adhesions. 3. Slight redness and congestion. 4. A dilated colon full of faeces. The prognosis in such cases is relatively favourable compared with that of true perforation, as out of 90 cases operated on 51 recovered—a mortality of 43·3 per cent. as compared with a mortality of 89 per cent. after operation for perforative peritonitis.

Netter, Mozer, and Salanier report four cases of **suppurative arthritis** in infants in which paratyphoid B bacilli were found in the pus. Their conclusions are as follows: The paratyphoid B bacillus may occur in pure culture in suppurative arthritis. This form of arthritis appears to be most frequent in infants in whom it may attack one or several joints. It may clear up without leaving any organic or functional disturbance apart from any surgical intervention. As a rule paratyphoid suppurative arthritis occurs in the course of an infection accompanied by digestive and respiratory symptoms. In some cases the joint manifestations of paratyphoid B may be of a milder character and not end in suppuration. The condition is then liable to be mistaken for rheumatism.

At the Medico-Chirurgical Society of the 14th region Serre and Brette reported two cases of **orchitis** and **epididymitis** in men aged 22 and 30, respectively, following paratyphoid fever B, the diagnosis of which was confirmed in one patient by blood culture and in the other, who had not been inoculated, by a positive Widal reaction (1:250). The complication occurred at the commencement of convalescence in one case and in the other 25 days after the temperature had become normal. In both cases the orchi-epididymitis was unilateral, there was no effusion into the tunica vaginalis and the vas deferens was not increased in size. In 8–10 days the temperature which had risen to 102·2 became normal, and recovery took place without atrophy of the testicle. There was no urethral discharge as in the case of paratyphoid A orchitis reported by Faroy (vide *Medical Supplement*, 1918, **1,** 131 *b*). In the subsequent discussion Cade stated that in conjunction with Vaucher and Huchon he had published five cases of genital complications in enteric fever, two of which were due to the typhoid bacillus, two to the paratyphoid B bacillus, and one to paratyphoid infection, the nature of which was not determined. The orchi-epididymitis which was always unilateral, with or without involvement of the cord, occurred in four cases during convalescence, and in one at the height of the disease. In both the cases of paratyphoid B infection suppuration took place. None of the cases showed signs of coexistent infection of the urinary tract.

In an article on the epidemiology and clinical aspects of paratyphoid fever A in Volhynia Silbiger states that the cases were of southern and western origin (Balkan and Italian fronts). In all probability the spread of the disease took place by contact infection. There were no grounds for the support of Schottmüller's view that food served to convey infection. The following clinical features were in favour of a diagnosis of paratyphoid A: an intermittent and remittent temperature and the wide distribution and character of the rose-spots which were more papular than maculo-papular. The gastro-intestinal and dysenteric symptoms seen in previous outbreaks were less common. In contrast with typhoid fever mild forms predominated. On the other hand, the complications and sequelae of severe attacks indicated that the disease was no less serious than typhoid or paratyphoid B fever.

Fernannini records a unique case of paratyphoid A in a soldier in whom the disease was complicated by mitral incompetence, myocardial degeneration, and diffuse chronic nephritis.

The **vesical symptoms**, due to the use of urotropin in the treatment of typhoid fever, are described by Roger, who classifies them as follows: (1) A first stage characterized by albuminuria connected with desquamation of the vesical mucous membrane and extravasation of pseudo-albumin. (2) A second stage in which the albuminuria is more pronounced and is accompanied by the presence of a few red cells. (3) A third stage with definite haematuria and evidence of vesical irritation. (4) A fourth stage, of which Roger's case was an example, characterized by actual cystitis. The most probable explanation of the injurious effect produced by urotropin is the irritation of the urinary passages by the two products ammonia and formic aldehyde into which urotropin is decomposed in the system.

Antityphoid inoculation. Friedberger, who is sceptical as to the value of inoculation against typhoid and cholera, regards the diminution in infectious intestinal diseases in the recent war as compared with former wars, as principally due to the same factors which caused a 10–30-fold decline in these diseases during the last decennia, viz., improvement in hygienic conditions.

He attributes the frequency of mild cases in inoculated soldiers, in contrast with the severity of the disease in the uninoculated civilian population, to the fact that in military statistics practically all cases were included. whereas, in the civilian population, only the severest are taken into account.

Of 80 cases studied by Lehmann, in which typhoid fever was contracted after inoculation, 20 were mild, 25 moderate, 28 severe, and 7 toxic. 12 died—a mortality of 15 per cent. The course of the disease in those who had been inoculated three times in no way differed from that in the uninoculated. All the classical symptoms of typhoid fever were present in their entirety and there was no change in the nature of convalescence. Relapses occurred in 20·75 per cent. of the severe and moderate cases. Toxic cases, which in six out of seven cases were fatal, were found among those who had been inoculated three times. The interval between the last inoculation and the first signs of the disease, which was 52·8 days on the average, did not appear to have any influence on the severity of the individual cases, the interval in the mild cases being 50·8 days, in the moderate 50·7 days, in the severe 54·5 days, and in the toxic cases 54·9 days. Lastly, no relation was found to exist between the character of the vaccinal reaction and the severity of the disease. Very severe and even fatal attacks of typhoid might occur after an inoculation accompanied by a very sharp reaction, and very mild attacks might succeed inoculations in which there had been no reaction at all. Lehmann concludes that any form of typhoid may occur even after three inoculations, and that in spite of inoculation death may be due not merely to complications but to the severity of the infection. Without wishing to generalize as to the value of antityphoid inoculation from so small a number of cases, Lehmann points out that to attribute the diminution in the incidence and severity of typhoid to inoculation would be to ignore the fact that every epidemic after reaching its acme tends gradually to subside spontaneously, and that the complete inoculation of the German Army coincided with this decline. Moreover there was a progressive improvement in hygienic measures during the war.

According to Randolph the evidence furnished by the Walter Reed General Hospital indicates that in rare instances latent infections may be made active by immunizing procedures, especially in those harbouring tubercle bacilli and streptococci. In very rare instances there may be an acute and even fatal reaction of the nature of anaphylaxis. Randolph records a series of cases showing various morbid conditions arising in connexion with inoculation of typhoid vaccine, viz., tonsillitis 2 cases, bronchitis 6 cases, broncho-pneumonia 1 case, fatal, arthritis 5 cases, tuberculosis 3 cases, inguinal adenitis 1 case, albuminuria 1 case, colitis 1 case, gastroenteritis 1 case, fatal, appendicitis 3 cases.

Guillain and Barré report a typical case of Landry's paralysis in a previously healthy soldier aged 31 following an injection of 1 c.c. of T.A.B. vaccine. Death took place after 10 days' illness. The condition had not been preceded by any acute illness, and the man had not been bitten by a mad dog or cat, so that rabies could be excluded. The onset of the symptoms in a perfectly healthy man on the evening of the day on which he had been given an injection of T.A.B. vaccine seemed to indicate a causal connexion between the injection and the toxic symptoms observed. Preti also reports two cases in which the symptoms occurred so soon after inoculation as to suggest a causal connexion. In the first case the vaccination was followed by an intense and prolonged reaction during which almost complete blindness developed. On examination of the eye six months later optic atrophy was found indicating that the initial process was optic neuritis. In the second case 10 days after the inoculation, frequent clonic convulsive movements of the left arm and face developed, being probably due to a circumscribed encephalitis of the cortex in the right Rolandic area. Pilcz relates 7 cases of nervous or psychical disturbance immediately following antityphoid or cholera inoculation and consisting in right hemiplegia with Jacksonian attacks, typical epilepsy, amentia of several weeks' duration, acute mania and cerebrospinal meningitis. He also alludes to cases of epileptic attacks following antityphoid inoculation reported by Bonhoeffer. In one case the patient, whose brother was an epileptic, had an attack half an hour after inoculation. In another case in which there was a previous history of epilepsy, several inoculations had no bad effect, but the last inoculation produced an attack.

Diagnosis. Paulicek attaches considerable diagnostic value to a peculiar bluish-red discolouration of the lips which is chiefly met with in mild and moderate attacks of enteric fever in which the diagnosis is difficult owing to the scarcity of the symptoms, whereas in severe cases the sign is absent or not well marked. It is not found in any of the diseases likely to be mistaken for enteric fever such as septicaemia, miliary tuberculosis, endocarditis, influenza, malaria or typhus, but is not infrequent in tuberculous disease of the apex. It is only rarely, however, that these two conditions are liable to be confused, and in such cases the progress of the disease will soon clear up the difficulty.

Brösamlen investigated **Widal's reaction** in normal persons and typhoid patients with the following results: (1) In 482 healthy persons who had received three antityphoid inoculations the reaction was positive in 358, or in 74 per cent. (2) The frequency of the reaction depended essentially on the time elapsed since the last inoculation. 14 days to three weeks after inoculation the reaction was positive in all cases; in one to three months after inoculation it was positive in 95 per cent. The frequency of the reaction then slowly declined, but was still positive in 56 per cent. at the end of the first year, and in 41 per cent. at the end of the second year. (3) Nothing final could be stated as to the duration of the reaction. It was certain, however, that it could last longer than two years. In 24 cases in which inoculation had been performed more than two years previously eight cases, or 33 per cent., gave a positive reaction, in one instance in a dilution of 1 : 1,000. (4) The height of the agglutination titre does not show any regularity. High titres of 1 : 500 or over are chiefly found in a period up to five months after inoculation. In Brösamlen's cases the highest titres were found four weeks after the last inoculation. This does not, however, prevent very high agglutination titres being found even later, e. g. even 1 : 1,000 30 months after inoculation. The height of the titre depends on a number of factors: (*a*) the time elapsed since the last inoculation, (*b*) the method employed, (*c*) the agglutinability of the typhoid culture used, (*d*) the variety of the vaccine, (*e*) individual differences in the intensity of antibody formation. (5) Widal's reaction in those who have been inoculated only possesses diagnostic value when the blood is examined at short intervals. A very rapid and steep rise of the agglutination curve is characteristic of typhoid if at least 3 months have elapsed since the last inoculation. The probability that the case is one of typhoid is all the greater the longer the interval since the last inoculation.

Prognosis. In a discussion of the comparative prognosis of the various forms of enteric fever, Gautier and Weissenbach state that in peace time the mortality from typhoid was 12·44 per cent., and during the war rose to 20·25 per cent. before inoculation. During the first three months of the war when few cases of paratyphoid were observed it rose to 37·5 per cent. As the result of the progressive disappearance of typhoid the mortality rate sank to 2·51 per cent. Paratyphoid A fever proved decidedly more frequent than paratyphoid B in the proportion of 3 to 1. Its mortality was always low, being only 1·4 per cent. according to Boidin, Merklen and Trotain. The mortality of paratyphoid B was decidedly higher, viz., 6 per cent. according to Boidin, and 11 per cent. according to Merklen and Trotain.

Treatment. Stein treated 500 cases of typhoid fever with sensitized vaccines prepared according to Besredka's method and found that in the great majority of cases it shortened the duration of the disease and convalescence and presented hardly any risk. In 84 per cent. the treatment had a distinct influence on the disease and in 10 per cent. it was ineffective. The mortality was 6 per cent. The large doses of 1–4 c.c. hitherto recommended for each injection were not found to be necessary. As a rule four injections, each containing 0·5–1 c.c. or 250–500 million bacilli were sufficient, sometimes only one or two were enough. The subcutaneous or intramuscular method produced little if any local reaction and no general disturbance whatever, and was therefore preferable to the intravenous method, especially in hospitals insufficiently staffed and with a large number of patients. As subcutaneous or intramuscular injection of a curative vaccine is not more dangerous than prophylactic inoculation, it is suitable for treatment of typhoid on active service and should be employed before the result of bacteriological examination is known or even when it is negative, if the clinical symptoms, especially a positive diazo reaction and the absence of urobilinogenuria, are in favour of typhoid.

Out of 50 cases of typhoid fever observed by Salmont in Thiroloix's service at La Pitié, vaccine treatment appeared to make the attack mild and of short duration in 34. In 13 of the 34 cases the temperature became normal in less than eight days after vaccination. Nine of these patients came under treatment during the first week of their illness, but four were admitted on the 10th, 13th, 19th, and 20th days respectively with severe attacks. In 12 cases the temperature fell in from eight to twelve days under the influence of vaccine treatment. In nine cases the disease was somewhat protracted, the temperature not becoming normal till 15–20 days after injection. But even in these cases the good effect on the general condition and the partial fall of the temperature after vaccination showed that the course of the disease was favourably affected. Of the remaining 16 two had a rapid fall of temperature after vaccination, followed by relapses which in both cases were complicated by intestinal haemorrhage. In seven the vaccine treatment had no effect. In two severe cases the symptoms became aggravated after vaccination, and death took place in 4 and 6 days respectively. In two death was due to intestinal haemorrhage, and in three to superadded infections.

The vaccines used in Salmont's cases were partly Vincent's polyvalent vaccine and partly autolysats. A subcutaneous injection of $\frac{1}{2}$ c.c. or 200 million bacilli was given on admission, and in most cases a second and third injection of $\frac{1}{2}$ c.c. was repeated with 12 hours interval between each. The patient was not given another injection till the temperature fell to 98·6 F. when he received another 200 million bacilli. Vaccine treatment is contraindicated in very severe attacks, and in those in which the myocardium is affected or the spleen is much enlarged.

Nichols, Simmons, and Stimmel record the results of surgical treatment of six chronic typhoid carriers. One, a urinary carrier was cured by nephrectomy, three 'intestinal' carriers were cured by cholecystectomy, and in two other cases of intestinal carriers this operation failed to cure the carrier condition. In the cases of the intestinal carriers the diagnosis and conclusions were based entirely on the outcome of cultures of the duodenal contents rather than on cultures of the faeces. The writers' conclusions are as follows:

(1) So called 'urinary' typhoid carriers are really kidney carriers and can be cured by nephrectomy. An additional argument for operation is present if the infected kidney is functionless.

(2) 'Intestinal' carriers are really bile-passage carriers of two kinds: (*a*) Cases in which the gall-bladder alone is affected. These can be cured by cholecystectomy, (*b*) Cases in which the gall-bladder and bile-passages are both infected. In these cases, of which the writers describe two examples, cholecystectomy does not cure the carrier condition, and the condition is incurable at present.

(3) The surgical treatment of typhoid carriers while not perfect is the best available.

van Berckel records a case of typhoid cholecystitis in a boy of 14. Cholecystectomy was performed and about 40 gall-stones removed. The operation, however, was not successful in ridding the patient of typhoid bacilli, as they were found in the stools two months and four months respectively after the operation.

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PNEUMONIA

At Camp Dodge, Iowa, during the month of October 1918 the total strength was 32,956 and 700 died of pneumonia following influenza, a mortality of 21·2 per cent. amongst those that had influenza. From September 16th to December 15th, 1918, Edgerly, Manson, Dwinell, and Carr report that there were 10,041 cases of influenza and in 2,800 patients pneumonia developed. The mortality from pneumonia was 26·6 per cent. For white and coloured troops it was about the same. The highest death rate was on October 12th, when 82 cases died.

Carr describes in some detail the **clinical aspects** of 274 cases of pneumonia in influenza seen at Camp Dodge. A high temperature at the onset of influenza should serve as a warning signal, for 62 per cent. of the 274 cases resulting in pneumonia had an initial temperature of over 104°. In only 4·17 per cent. of 127 cases of influenza that did not develop pneumonia, was the early temperature above 104°. In considering the question of the relationship of the temperature curve and the onset of pneumonia Carr distinguishes four classes of cases: (1) Continued high fever with gradual development of symptoms and signs of pneumonia; (2) Following a drop below 102° there was a secondary rise of temperature often accompanied by expectoration or sometimes a chill; or sharp pain in the chest or abdomen occurred with the onset of pneumonia; (3) A less frequent type with a steady decline of the temperature curve usually accompanied by a moderately extensive pneumonia terminating quite early by lysis; (4) A small class in which the chart showed an irregular curve throughout. Carr points out that the extent of involvement of the lungs, as shown at autopsy, is often much wider than was suspected clinically. Crisis occurred in 14·7 per cent. of the cases of pneumonia. As factors in the production of cyanosis, Carr suggests: (1) an overwhelming toxaemia depressing the vasomotor centre; (2) the extent of the pulmonary lesions sufficient in itself to produce death practically by suffocation, and (3) in a large number of cases macroscopic changes were seen (at autopsy) in the adrenals and it is possible that adrenal insufficiency may cause an early collapse of the patient. Carr points out that the signs may persist in the lungs for some time and patients should not be discharged from hospital too early and should be protected from exposure and undue activity for some time after apparent recovery.

Greenway, Boettiger and Colwell have reviewed their experience with 2,344 cases of pneumonia and its complications seen at Camp Bowie, in the United States, from the opening of the Base Hospital on September 24th, 1917, to January 1st, 1919. The cases fall into three distinct groups. In Group I from September 24th, 1917, to January 1st, 1918, during a widespread epidemic of measles there were 973 cases. 237 died; a mortality of 24·4 per cent. Empyema was present in 17 per, cent. of the cases, with a mortality of 32·5 per cent. In Group II from January 1st, 1918, to September 27th, 1918, there were 538 cases with a mortality of 7·4 per cent., and 9·4 per cent. developed empyema with a mortality of 37·5 per cent. In Group III from the beginning of the epidemic of influenza on September 27th, 1918, to January 1st, 1919, there were 3,876 cases of this disease. No patients died of uncomplicated influenza. Pneumonia developed in 833 of the cases of influenza, and 156 died, a mortality of 18·7 per cent. and 4·3 per cent. had empyema with a mortality of 11·5 per cent. of the total deaths. These authors show by means of charts certain striking contrasts in the pneumonias that followed measles and those that occurred after influenza. In Group I the curve showing the number of cases of pneumonia exhibited its first peak two weeks after the beginning of the epidemic of measles, and sometimes in individual cases pneumonia did not supervene until several weeks after an attack of measles. In this group also, involvement of the pleura was often the initial and outstanding feature. In Group III the first peak of pneumonia showed itself only 5 days after the beginning of the epidemic of influenza, and signs of consolidation of the lungs were rarely found for the first time later than five days after the onset of the attack of influenza. Sometimes the symptoms in the cases of both groups suggested meningitis for the first twenty-four hours, but the cerebrospinal fluid was negative. The majority of the cases in Group II were of the ordinary type of lobar pneumonia so well known in civil life, which comes on after exposure. Here there was no history of previous infection. During the first five days of pneumonia in the cases of Groups I and II 85 per cent. of the patients had white blood counts of over 10,000 and the percentage of polymorphonuclears was 70 or more. On the other hand, in Group III, in the cases of pneumonia following influenza, 60 per cent. of the counts were below 10,000, and in 35 per cent. of these cases the percentage of polymorphonuclear leucocytes was under 70. The average length of illness in the fatal influenzal pneumonias was 11 days, being much shorter than it was in the first two groups in which it was 21 days. The authors give a table setting forth in the light of post-mortem findings the difficulty of diagnosing lobar from confluent broncho-pneumonia. The conclusion is drawn from this fact, that statistics of these two types of pneumonia, diagnosed as such during life, are not reliable. Even at autopsy differentiation of these two forms was very difficult on some occasions.

Lorrain, Hanns, and Gillet give an account of 7 cases of '**pseudo-tuberculous pneumonia**' as they term it; cases of pneumonia caused by the pneumococcus, but of a subacute type, with delayed resolution, or which for some other reason might easily be taken for pulmonary tuberculosis. The first patient, seen in 1916, had a history suggestive of tuberculosis, namely 'intercostal neuralgia' on both sides of the chest, but especially on the left, in 1914; in 1915 'pleurisy left', and he was in poor health until his admission into hospital in 1916. He then had dullness at the left apex, fine râles, and here the breath sounds were poorly heard. He also had haemoptysis and severe diarrhoea with mucous stools containing a little blood. His temperature registered between 102° and 104° for ten days. For two weeks more he had fever between 100·4° and 102°, falling in three days' time to normal. On three occasions no tubercle bacilli were found in the sputum but only pneumococci. In a week more the lung had cleared up. The Widal reaction was negative. Seen three months later the patient was quite well and the chest negative. Without being able to state confidently that this patient was not tuberculous, the writers feel that they can affirm that the illness in 1916 was not of a tuberculous nature. Four cases of a second type are described, a pneumonia or broncho-pneumonia with delayed resolution with persistent fever, or a pneumonia incompletely resolved exhibiting relapses. These were probably due to some foci of infection, with colonies of pneumococci giving rise to slight fever and causing cough and expectoration. In none of these were tubercle bacilli found. In a third class two cases are given, where, in spite of the fact that nothing could be found in any other system and because of pulmonary symptoms with cough and abundant expectoration (but no auscultatory signs) accompanied by progressive emaciation, one was forced almost to the diagnosis of tuberculosis. But again no tubercle bacilli were found and only pneumoccoci. One of these patients had been 'gassed' and the writers draw attention to the frequency with which prolonged subacute infections due to the pneumococcus, may supervene upon the inhalation of asphyxiating gases. A very good summary is given of the literature of prolonged or relapsing pneumonia from the time of Charcot's graduating thesis in 1860 up to the present day. Many cases have been reported as following upon influenza. The final criterion as to diagnosis, in the minds of these writers, rests upon the exclusion of tuberculosis by repeated examinations of the sputum. Finally it is emphasized that the possibility of 'pneumopathies pseudo-tuberculeuses à pneumocoques' must be borne in mind. The writers say that tuberculosis specialists in the army are too prone to see tuberculosis in every case. In the opinion of the reviewer, the safest plan for the physician, face to face with such cases should be to reserve the diagnosis of 'unresolved pneumonia' till the very last and only fall back upon it when none other can be supported. Perhaps the final chapter in the history of the patients described above has not yet been written.

Between September 1st, 1918, and January 1st, 1919, Levin, Goodman, and Pancoast examined the **urine** of 1,082 patients suffering from pneumonia or influenza. Of these 11·18 per cent. contained albumin alone and 18·30 per cent. showed albumin and casts. In 70·52 per cent. of the patients the urine was normal.

Greenway, Boettiger, and Colwell discuss the complications of 2,344 cases of pneumonia. In the group of cases following the epidemic of measles empyema occurred in 16·5 per cent. of the pneumonias, whilst it was found in only 4·3 per cent. of the influenzal pneumonias. Chills and sweating were very rare and physical signs were uncertain. In summing up they write, 'in our experience dullness, with a change in breath and voice sounds, sometimes a diminution, more frequently bronchophony or aegophony, are the best indications for requesting a Roentgen-ray examination even though this may be limited to a fluoroscopy'. They never hesitated to put a needle into the chest once or many times if there was any suspicion that pus was present. Stress is also laid upon the difficulty of finding the pus owing to the tendency towards the formation of adhesions and pockets in the pleural cavities of these patients. Carr also points out the difficulty of diagnosing empyema and cites one case where 'fluid was suspected and four days later the beginning of resolution was present and on the following day this patient died'. Greenway, Boettiger, and Colwell noted generalized subcutaneous emphysema as a complication in 8 cases and 3 of these recovered after a prolonged convalescence.

Pathology and Bacteriology. MacCallum's paper and also his monograph published by the Rockefeller Institute for Medical Research are splendid examples of that abundance of work which has been done in the United States on pneumonia as it occurred in the large army camps before and during the time of the influenza epidemic. In the years 1917 and 1918 there was an enormous amount of pneumonia and comparatively little of it could be described as of the classical lobar type. On the other hand, the form of pneumonia generally met with was quite different in character. The majority of cases occurred in soldiers who had just had measles, but it must be admitted that some of the cases were not preceded by an attack of this disease and yet they too had the same atypical form of pneumonia. The cases following upon measles were studied by MacCallum at San Antonio, Texas; later at Camp Dodge, Iowa, where there had been no epidemic of measles, he investigated a large number of cases of pneumonia. In both instances the *Streptococcus haemolyticus* was the predominant micro-organism found in the lungs—although *Bacillus influenzae* was often present in the upper air passages—and in the later cases staphylococci, pneumococci and miscellaneous bacteria were found in the lungs. By bitter experience it was learned that the haemolytic streptococcus was the micro-organism to be greatly feared and that patients with measles, who harboured this organism in their throats, were a dire menace to the other cases of measles in the same ward. By isolating such patients from the others, the incidence of pneumonia due to haemolytic streptococci was greatly lessened.

The outstanding feature in the lungs, if the resistance of the patient to the streptococcus had been great, was a form of nodular broncho-pneumonia which extended along and about the bronchioles 'so as to present itself upon the cut surface of the lung in the form of branched grey opaque projecting foci surrounded by areas of haemorrhage, oedema and collapse. Except in the earliest stages it was always accompanied by an effusion of fluid in the pleural cavities with a rather abundant exudation of fibrin. The most striking feature of this form of pneumonia is found in the rapid infiltration of the substance of the lung tissue with wandering cells and the new formation of connective tissue in the bronchial and alveolar walls, the interlobular septa and pleura, and even in the exudate which is found in the bronchi and adjacent alveoli. It is for this reason that the name interstitial broncho-pneumonia has been applied to it'. At the autopsies performed upon patients who have died after an illness of only a few days the bronchi are filled with an accumulation of leucocytes and streptococci, and the walls of the bronchi and the most adjacent alveoli are infiltrated with mononuclear cells. A few leucocytes are found in these air sacs with a large amount of blood, but rarely any streptococci. If the patients have lived for more than a week, there is usually a large collection of thin turbid fluid in one or both pleural cavities containing an enormous number of streptococci and the lung is covered with much shaggy fibrinous exudate. On section of the lung, nodules of pneumonia are seen with yellowish or brownish pus as centres (the contents of a bronchus). Outside this is the thickened grey wall of a bronchus which merges into the more yellow border of firmly consolidated tissue. Beyond this again are found rings of haemorrhage and oedema.

The really important point, which MacCallum so ably demonstrates, is that we are dealing here with an organism that meets with a high grade of resistance in the bronchi and bronchioles. It does not easily reach the alveoli by way of the lumen of the bronchiole and we find the alveoli affected only if the organism has extended through the wall of the bronchiole. The characteristic reaction to the invading organism is then to be looked for in the bronchus and in its outer coats and in the tissues which make up the interlobular septa. Microscopically it is seen that the bronchial walls are greatly thickened by infiltration of wandering mononuclear cells and by much newly formed and highly vascularized connective tissue. The alveoli which lie close at hand may be filled with fibrin, but contain few wandering cells and micro-organisms. Organization of the exudate in the bronchi and alveoli tends to take place rapidly. The lymphatics, which course through the walls of the bronchi and in the interlobular septa, are filled with thrombi, made up of a network of fibrin loaded with leucocytes and mononuclear wandering cells. These changes may be traced out along the septa and even into the pleura. Streptococci swarm in the bronchi and in the thrombosed lymphatics of their walls and grow out in the lymph channels of the interlobular septa, reach the pleura, and cause the pleurisy and the effusion. If the resistance to the invading organism is somewhat less, we find small areas of grey lobular pneumonia (the alveoli being filled with leucocytes and streptococci) *plus* the interstitial changes described above. Again, if the resistance is practically nil and no barricades of newly-formed connective tissue in the bronchial walls and in the adjacent alveoli are thrown up, a confluent streptococcal pneumonia results, for the micro-organisms gain ready access to the alveoli. In this case none of the interstitial changes are seen. Sometimes, in cases accompanied by much pleural effusion, quite large abscesses were found in the lungs, which were caused by streptococci alone or by a variety of bacteria. The streptococci rarely invaded the blood-stream and endocarditis was a rare finding, but pericarditis with a seropurulent effusion was more often seen. Rupture of the fibres of the rectus abdominis muscle, which had undergone hyaline degeneration, was sometimes found. Haemorrhage had also taken place between the ends of the broken muscle, and on some occasions this was infected by streptococci. Degeneration of the tubules of the testes with arrest of spermatogenesis was seen under the microscope at some of the autopsies.

In the autumn of 1918, at Camp Lee in Virginia, and also at the Johns Hopkins Hospital, Baltimore, MacCallum investigated the pneumonias which accompany or follow influenza. In both these groups of cases he found lobular pneumonia, which picked out only certain groups of lobules or affected a large number of lobules lying close together, so that a large mass of pneumonia was formed. Thus the individual lobules did not stand out in contrast with the relatively healthy ones. Occasionally even all the lobules of one lobe might be affected. MacCallum describes this condition as 'an extremely fresh pneumonia, qualitatively, but not in distribution, like the rather hypothetical stage of engorgement which precedes red hepatization in lobar pneumonia'. In the exudate of the bronchioles and of the alveoli lay scattered pneumococci, sometimes in small, at other times in enormous numbers, and the phagocytic cells were filled with them. Haemorrhage was always predominant in these lesions. Death had occurred rapidly through a pneumococcal infection. In other cases the haemolytic streptococcus was the predominant organism, and this outgrew all other bacteria which may have been present. A confluent lobular pneumonia was found corresponding very closely with that seen in those patients who had had measles and whose resistance to a streptococcal invasion was extremely low. On the other hand, in another locality (Camp Dix), where MacCallum also studied the pneumonias which occurred during and after attacks of influenza, the findings were of quite a different character. There the condition was one of interstitial broncho-pneumonia, but the lesion was caused by the *Bacillus influenzae* of Pfeiffer and not by the *Streptococcus haemolyticus*. The bronchi were filled with an exudate of polymorphonuclear leucocytes, many of which contained a large number of influenza bacilli, though numbers of such bacilli were extra-cellular in position. The neighbouring alveoli held leucocytes, some fibrin and epithelial cells, but no conspicuous haemorrhage, and the intra-alveolar exudate was undergoing organization. In contrast with the streptococcal interstitial broncho-pneumonia, however, the influenza bacilli were restricted to the bronchioles and were not shown in the air sacs; the lymphatics were inconspicuous and were not filled with thrombi loaded with bacteria; the pleural cavities were not affected as in the streptococcal cases; and organization of the exudate was an even more striking feature in the influenza cases. The same resistance to invasion by *B. influenzae* as to that of the haemolytic streptococcus was shown by the phenomenon of barricading with newly-formed connective tissue. In a very few cases there were examples of a 'local victory' for Pfeiffer's bacillus and a few patches of alveoli showed an exudate of leucocytes loaded with influenza bacilli. In other instances there was evidently at first an invasion by *B. influenzae* and only later by streptococci, which swarmed everywhere and produced a widespread haemorrhagic exudate into the air sacs. Still other cases showed staphylococcal forms of lobular pneumonia.

MacCallum, in summing up, compares measles with influenza and states that both diseases are of unknown causation, but both produce a very depressing effect upon the resistance of the individual, allowing of the invasion of the lungs and the production of pneumonia by such 'secondary invaders' as the haemolytic streptococcus, the influenza bacillus, the pneumococcus, and the staphylococcus. An extraordinarily varied picture may thus result, especially if one of these 'secondary invaders' follows another one. Now one, now another of these organisms may predominate in one section of the country, or the predominating one may even change in the same locality, and this fact accounts for the different reports as to bacteriological findings.

Schorer, Clark, Sanderson, Dickson, and Huntoon give an account of the pathology and bacteriology of cases of pneumonia and empyema which occurred at the Base Hospital at Camp Merritt, a hospital which received soldiers taken ill just before they were ready for embarkation for Europe. The series comprises those ill between February 25 and May 15, 1918. Very few cases, in contrast with those of Cole and MacCallum, followed upon measles or other epidemic diseases, and at this time influenza had not yet appeared. The variety of pneumonia found was lobar (151) and interstitial broncho-pneumonia (28), but in two instances these two types were combined. These investigators believe that the pneumococcus causes most of the lobular pneumonias of civil life, and that the *Streptococcus haemolyticus* causes the interstitial broncho-pneumonia. MacCallum's picture of this latter form may be taken to describe the cases at Camp Merritt also. The bacteriological work done on these cases is very complete. It is shown that very often a pneumococcus (of any one of Avery's types) might be combined with a haemolytic or non-haemolytic streptococcus in the sputum of patients suffering from either lobar or interstitial broncho-pneumonia even where care was taken to obtain a specimen of sputum, not from the throat, but from the lower air-passages. Also amongst these cases of pneumonia there were 13 where cultures produced neither a pneumococcus nor a streptococcus, but the influenza bacillus or another Gram-negative bacillus. These writers employ a clinical diagnosis in dividing the cases into 'lobar' or 'broncho-pneumonia', but it may be objected that this clinical classification is not sufficient when the end in view is to collect bacteriological data. For this reason, the value of the statistics is greatly decreased. In support of this objection it is rather remarkable that of the cases caused by a haemolytic streptococcus alone, 31 were of the lobar and 12 of the broncho-pneumonic type, and caused by a non-haemolytic streptococcus alone there were 20 'lobars' and 4 'bronchos'. If a post-mortem classification were employed, it seems very possible that the proportions would be reversed. Indeed, we are not told how many autopsies were done on these cases. At the time of writing the paper 42 of the patients had died, 60 had been sent away presumably cured, and 70 remained in the hospital. In this series of cases 81 had fluid in the pleural cavity, and 56 of these had purulent pleural exudate. Empyema was a little more common in the cases of haemolytic streptococcal pneumonia than in the pneumococcal pneumonias. And the rôle of the haemolytic streptococcus in the causation of empyema is more clearly demonstrated when it is realized that 'in spite of the fact that in 116 cases of pneumonia in which we found type pneumococci, 22 out of the 26 empyemas were caused by haemolytic streptococci'. In the view of the writers, the *Streptococcus haemolyticus* is rarely the primary cause of pneumonia, but it assumes an important position in bringing about the final results. Elaborate tables of the cultural reactions of the different strains of streptococci on various sugar media are given, and the authors show how an antiserum may be produced. This is used in demonstrating a precipitin factor (soluble in bile) which is elaborated by the haemolytic streptococcus.

Dwinell reports the results of the bacteriological examination of the lungs from 53 autopsies performed by Brumbaugh between October 3 and October 11, 1918, at Camp Dodge, Iowa. The *Streptococcus haemolyticus* was recovered in 80·7 per cent., from lungs, pleural cavities, or from the heart's blood. In 52 per cent. of the blood cultures the result was positive for this organism. *Bacillus influenzae* was found in 9·6 per cent. of the cases, and in three instances in both lungs and pleural cavities. Once it was recovered from the blood and once from the peritoneal cavity. Four times it was associated with the *Streptococcus haemolyticus* and once with the *Staphylococcus aureus.* A non-haemolytic streptococcus was found five times and a staphylococcus twice. Dwinell considers that it was owing to 'poor technique in handling the cultures' that *B. influenzae* was isolated so infrequently, for in another series of 69 autopsies, a few weeks later, it was found in 49·3 per cent. of the cases.

Of great importance in connexion with atypical pneumonias caused by the *Streptococcus haemolyticus* is the question of carriers. Levin, Goodman, and Pancoast, during May, June, and July of 1918, selected 100 'apparently normal individuals, surgical and other patients not suffering from influenza or pneumonia'. In 55 per cent. of these, throat cultures for *Streptococcus haemolyticus* were positive, and 45 per cent. gave a negative result. There were very few cases of respiratory disease in the hospital at that time. They also noted that when patients, suffering from empyema or pneumonia caused by this micro-organism, were put outside in the open air and sunlight there was a marked decrease in the number of those who harboured the organism in their throats. When brought into the wards, however, there was a considerable increase in the number of carriers of the *Streptococcus haemolyticus.*

Myquist and Ross describe 13 cases of **subcutaneous emphysema** which occurred in patients suffering from pneumonia after influenza at Camp Hospital No. 12 with the American Expeditionary Forces. The mode of origin of this complication and the mechanics of its production have formed the subject of several papers. Numerous workers have reported from hospitals, where a large number of cases of influenza were treated, that a small percentage of patients showed subcutaneous emphysema, which appeared first at the root of the neck after broncho-pneumonia had become well established. The area of emphysema often spread up to the jaws, down over the chest and into the axillae. In one of the cases in the series of Myquist and Ross it extended down to the finger-tips and even below Poupart's ligament. The view supported by most authorities at the present time is that, owing to a marked interstitial inflammation and formation of small abscesses, air from the bronchi gets into the supporting tissues of the lung, and through coughing is forced along (taking the line of least resistance) in the connective tissue, in which lie the blood-vessels, and with these it passes to the hilum of the lung, where it readily spreads by way of the mediastinum up behind the sternum into the region of the neck. Myquist and Ross, whilst emphasizing the fact that the lungs at post-mortem examination showed numerous abscesses, do not seem to think that a mechanical theory for the spread of air, as outlined above, explains all the facts. On the other hand, they favour the view that the emphysema may be due to gas production in the subcutaneous tissues. A Gram-positive bacillus was isolated from the blood in two cases before death, and in four cases at autopsy from the heart's blood and gaseous tissues. This bacillus was non-motile, acid fast, grew in stab cultures but never on the surface, produced spores but possessed no capsule, and produced gas in secondary cultures after 48 to 72 hours. A culture was inoculated into the blood-stream of a rabbit, which was killed 15 minutes later and put into the incubator, and this caused a generalized infection with gas production. No definite grouping or classification of the organism was done. It is to be regretted that the writers do not tell us how long after death the autopsies were performed. They state that at the autopsies the gas had no odour, but do not say whether the gas formed by the bacillus is, or is not, odourless. Gas-producing bacilli are very frequently found in ordinary post-mortem work. It is of some interest to note that four of their cases were seen in one ward in the course of three days, but Myquist and Ross agree that this fact does not by itself justify the theory that the subcutaneous emphysema was of bacterial origin. Greenway, Boettiger, and Colwell made cultures from the mediastinum in their cases of subcutaneous emphysema. In eight cases a pneumococcus (group IV) was recovered, and a streptococcus in two cases. These organisms were also found in the blood. In the three remaining instances of emphysema there was no growth. No gas-producing anaerobe was found.

In the series of pneumonias following measles and influenza, described by Greenway, Boettiger, and Colwell, the lungs at autopsy showed the same picture as has been so well outlined by MacCallum. The type of pneumococcus was determined from the sputum and extensive bacteriological work was done at autopsy. The finding of *Streptococcus haemolyticus* in the lungs of cases of broncho-pneumonia and interstitial broncho-pneumonia was as frequent as reported by many other investigators. Their findings led them to the conclusion that 'definite evidence of the *B. influenzae* as a determining factor in pneumonias following the epidemic of the fall of 1918 was not obtained at this hospital'.

Hart has given an account of the cases of lobar pneumonia seen during the year ending July 1918 at the Presbyterian Hospital, New York. There were 121 cases in all, 96 of which were caused by the pneumococcus and 25 by various other organisms such as *B. influenzae*, *B. mucosus capsulatus*, and *Staphylococcus aureus*. Blood cultures were positive in 38 of the pneumococcus cases. Hart confirms the findings of Cole and his associates at the Rockefeller Institute, that a positive blood culture obtained during life indicates that a severe infection is to be expected. The organisms, obtained from the sputum or from the blood, were typed according to the classification of Avery; of type I there were 33 cases and 8 died; there were 30 of type II and 13 died; type III was represented by 10 cases and 6 died; type IV, 23 cases with 7 deaths. Positive blood cultures were obtained in 4 out of 6 fatal cases of pneumonia due to type III, which always causes the severest infection. In one of the other two fatal cases of this group the blood culture was negative, but in the other one no blood culture was done. All these figures are very much the same as in various other series recently published in the United States. Only the cases of type I infection were treated with specific anti-pneumococcus serum.

Menetrier describes the **gross pathology** of 400 cases of pneumonia, but leaves the discussion of the bacteriology and microscopic anatomy for a paper which is to be published later. All the autopsies were done before 'last May' (no year given), and were performed upon patients coming from an infants' ward and from the adults' wards, male and female, at the Tenon Hospital in Paris. The service, from which these cases came, consisted of more female than male wards, and this accounts for the fact that 199 females, in contrast with 201 males, died of the disease; thus showing a much higher proportion of the former sex than is usual in statistics. As no record of the living cases is given, it is impossible to draw conclusions of any great value from the table of death-rates arranged according to age. The author does point out that the mortality amongst nursing mothers was very high, and he states that 'almost all the women below the age of 30 [25 cases], who are shown in our statistics, with the exception of those who died during the epidemic of influenza, were stricken with the disease whilst nursing infants'. From this mention of influenza, and when we consider that the series was concluded in 'May', we must infer that some at least of the 400 autopsies were performed upon cases of pneumonia following that disease. If we are right in this assumption then the statistics lose much of their value. The author states that all were cases of lobar pneumonia, but it is well known that the majority of cases which follow influenza are not of lobar but of bronchial type, although areas of this latter lesion may coalesce so as to involve an entire lobe. Menetrier, indeed, divides the cases into two classes; primary pneumonia affecting persons in good health, and 'pneumonia secondary to affections of a more or less serious nature and often occurring in their final stages'.

It is only possible to pick and choose from the mass of facts presented in the paper. There were 187 instances of pneumonia confined to the right lung only. In 103 cases both lungs were affected. As is the general rule, the right lower lobe alone was most often involved; the disease was present only in this lobe in 62 cases. Of involvement of the left lower lobe alone there were 49 instances; of both lower lobes together, 23; and a lesion of all lobes of both lungs in 10 cases. All stages of the disease were seen, and in two instances, in the various lobes affected, engorgement, red hepatization, grey hepatization, and the stage of resolution are recorded. Amongst the various types of hepatization Menetrier distinguishes a haemorrhagic one, 'where the appearance of the lesion resembles that of an infarct, and these are observed particularly on the pneumonias of influenza.' This variety was recorded 12 times. Under the heading of 'anomalies in the evolution and complications of the pneumonic lesion' small multiple abscesses are recorded 8 times; large solitary abscess 5 times; gangrene 5 times; red infarct 7; arterial thrombosis without infarct 10 examples. Primary cancer of the lung was observed in one case. Any data on the association of tuberculosis with pneumonia are always of value, and Menetrier, in the 187 cases, where care was taken to look for tuberculous lesions in the lungs, noted it 78 times as seen with the naked eye. In 5 of these cases active tuberculosis was found in the areas of pneumonic consolidation, and in other parts of the lungs 21 times. Advanced tuberculosis with cavity formation was noted 6 times and miliary tuberculosis twice. Non-active or fibrous tuberculosis was present in 44 cases. Purulent exudate in the pleural cavity was found only on 5 occasions, but it is pointed out that post-mortem examinations were not carried out by the writer upon those patients who died after operation for empyema. Pneumothorax was seen in one case. Acute endocarditis due to the pneumococcus was present in 22 cases (in 5 of these upon valves already the site of disease) and was distributed as follows on the valves: mitral, 11; aortic cusps, 9; and on the tricuspid valve, twice. In 7 other cases there was acute vegetative endocarditis, but no micro-organism was demonstrated. Cardiac thrombi were present 4 times, twice in chambers on the left side, and twice on the right side. Arterial thrombosis due to the pneumococcus occurred 25 times, 19 times in the pulmonary, 5 times in the cerebral, and once in the popliteal artery. Menetrier noted fatty degeneration of the liver, visible to the unaided eye, in 219 cases. The spleen was enlarged in 16 cases, and recent infarcts were seen 5 times. Fibrino-purulent pneumococcic meningitis occurred in 10 cases, in 4 of which endocarditis was also present. Purulent pneumococcic peritonitis and multiple suppurating pneumococcic arthritis were each found once.

Turck has done some interesting work on **experimental pneumonia** in animals, the results of which seem to have a wider significance than merely for the particular disease in question. He claims that the ferments of the micro-organism (trypsin, pepsin, and erepsin) do not cause the lesion directly, but that these must first digest the cells of the animal, and the toxic products resulting from this digestion produce the disease. His method of causing pneumonia is to allow the lungs of cats (in a sterile chamber containing chloroform vapour) to undergo autolysis; no bacteria are found, either microscopically or by culture, in this autolysed tissue. It gave a strong biuret reaction. A small amount (0·5–1 c.c.) of this emulsion was introduced by means of a special tube into the trachea of a cat. In some cases the animal died in the course of four minutes; in others typical lobular or lobar pneumonia resulted. In those cats that died quickly, foci of haemorrhage were found in the lungs; and in some instances the lungs were soaked with blood. Whether death occurred immediately or whether pneumonia was produced, depended upon the amount of the toxin which reached the finer bronchioles. It is interesting to note that the trachea and bronchi appeared quite normal in the earlier stages of the pneumonia. Identical pneumonias could be caused by intravenous injections of homologous lung tissue autolysed *in vitro*; reaching the alveoli, therefore, by way of the capillaries and not through the air-passages. It is essential in both cases that the toxin should reach the epithelium of the alveoli, and here the primary lesion is produced. Cats' paws were covered with a thin paste of the autolysed lung tissue. In a short time the animals began to sicken, and eight out of the ten cats died of pneumonia, from 48 hours up to one week after the application to their paws. As controls, tracheal insufflation of cats with autolysed lung tissue of dogs, sheep, rabbits, and horses, and application to the paws of cats was done, but no pneumonia resulted. This proved to Turck that homologous lung tissue must be used. If the throat of a cat were sprayed with pneumococci, no pneumonia was produced and the animals did not die. In a certain number of animals chloroform insufflated into the trachea caused destruction of lung tissue and pneumonia. Pneumonia could also be brought about by subcutaneous injection of autolysed lung tissue. Turck writes that in the treatment of disease due to bacteria an effort must be made to immunize the patient to digested or autolysed tissue-products instead of to the bacteria themselves. He reports certain experimental work, which he has done in producing protective and curative sera. Thus injections of autolysed human tissue in the course of six months will stimulate the production of specific antibodies. He also reports favourably on the benefits of treatment with such sera, but in his paper does not go into details.

Treatment. Hart describes the results of treatment by means of anti-pneumococcus serum in 33 cases of lobar pneumonia due to type I pneumococcus (Avery). As soon as the organisms obtained from the sputum were typed the treatment was begun by employing the method advocated by Cole and his associates in 'Acute Lobar Pneumonia', *Monographs of the Rockefeller Institute*, No. 7, 1917. Serum obtained from this Institute or from the New York Board of Health was used. The patients were first tested for sensitiveness to foreign proteins by an intradermal injection of 0·02 c.c. of sterile horse serum diluted with 9 parts of normal saline. If the patient was sensitive—a large urticarial wheal appearing in a few minutes' time—he was desensitized by subcutaneous injection of increasing doses of antiserum, at half-hour intervals, beginning with 0·025 c.c. If no reaction follows 1 c.c., then intravenous doses, the initial dose of 0·1 c.c. being doubled every half hour. If a general reaction occurs no dose should be given for 2–4 hours. After 25 c.c. have been given in small doses 4 hours are allowed to elapse then 50 c.c. are given. In 19 of the cases treatment was begun within 12 hours of admission to hospital, and the remainder of the 33 cases received the first dose more than 24 hours after admission. The first dose consisted of 90–100 c.c. of antiserum. Every 8 hours this dose was repeated if the temperature remained above 102°. Two patients received only one dose of 100 c.c. as the temperature soon dropped. In 4 cases as much as 1,000 c.c. in all were given. The same reactions were observed as have been described at the Rockefeller Institute. *Early reactions* were seen in 15 cases, but in 7 of these they were slight. In others no great alarm was felt, although extensive urticaria, dyspnoea, cyanosis, quickening of the pulse, and sometimes cough, vomiting, and headache occurred. An injection of adrenalin at once relieved these symptoms. A *thermal reaction* (a rise in temperature), with or without a chill, occurred in 6 cases, sometimes after the initial dose, or after the second; in one instance it followed the fifth. *Late reactions* were observed in all but 2 cases, 10 mild, 6 of a medium and 9 of a severe grade. This true 'serum sickness' came on usually about 6–7 days after the last dose. It terminated in some cases after 2 days, but lasted much longer in the severe reactions, and several patients showed disturbances for even 3 weeks. There was no relation between the severity of this late reaction and the amount of serum given. A mild late reaction revealed itself only by a slight urticaria and moderate enlargement of the superficial lymph nodes. In the severer grades of serum sickness there was marked and prolonged urticaria, extensive erythema, fever, pronounced enlargement of the lymph nodes, subcutaneous oedema, and hot, swollen, tender joints, as in rheumatic fever. A moderate grade of eosinophilia resulted. Some of the patients seemed very ill for a few days, but all recovered from the reaction. A number of the patients had an irregular fever of 101°–102° for from one to three weeks. In these cases the possibility of empyema was excluded. The number of cases is small, but one of the most marked benefits derived from the treatment of these patients was that the blood became sterile after the first, second, or third dose in those instances where a positive blood culture had previously been obtained. Some of the examples are very striking in this regard. It must be borne in mind that this disappearance might have been due to a natural recovery of the patient. In 3 of those patients, in whom a sterile blood was not obtained in cultures after the treatment, an acute endocarditis was found at autopsy in 2 cases, the third patient left the hospital and could not be traced, and in a fourth instance an empyema was found. Two cases received the first dose on the 2nd day of disease, 2 on the 3rd, 8 on the 4th, 4 on the 5th, 4 on the 6th, 2 on the 7th, and 1 on the 8th day of disease. Crisis occurred in 12 cases; for the earlier ones on the 3rd to 6th day; in the later cases on the 7th day. Where the treatment was not commenced until the 8th day the patient had his crisis on the 11th. In 11 instances recovery occurred by lysis, beginning on the 4th to 7th day of disease according to the time that specific treatment was commenced.

Hart has never previously seen in various series of untreated cases the extraordinary and prompt improvement noted above. No specific treatment was employed in other cases of pneumonia, caused by types II, III, and IV, as no efficient antiserum to these types has yet been found.

Greenway, Boettiger, and Colwell strongly recommend that patients suffering from pneumonia should be isolated if possible to prevent superadded infection by other organisms. The 'secondary invaders' were an outstanding feature of the pneumonias following influenza. These writers treated 125 cases of pneumonia, due to type I pneumococcus, with antiserum specific for that type and only 7 died, a mortality of 5·6 per cent. Even in these fatal cases death must be attributed to empyema. Seventeen cases of type I infection were not treated and none died. These did not receive antiserum on account of the mildness of the infection, and in some instances because, owing to delay in being sent to hospital, they had their crisis before the type of pneumococcus could be determined. The earlier the antiserum was used, the more striking were its effects. A few patients were sensitive to horse serum, but none of these were very ill after antiserum was used. These workers strongly endorse the employment of the serum in type I infection. All their patients received digitalis. In the treatment of empyema repeated aspiration is recommended, followed by resection and drainage, if necessary, after adhesions have formed. This is also the opinion of the American Empyema Commission. Speaking of early operations in empyema, Greenway, Boettiger, and Colwell say 'these operations, performed at the height of toxaemia, meant death either from shock or asphyxiation'. Post-operative care should be in the hands of a physician, and in their opinion the patient should be kept on the medical side with an 'enthusiastic well-qualified surgeon to carry out the irrigation and dressings'.

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A. M.

SYPHILIS

Symptomatology. The symptomatology of latent and occult syphilis is discussed by Hubert; a valuable and thoughtful article. For three and a half years a routine Wassermann test has been performed on every patient attending the Medical Clinic in Munich to which he is attached. A positive Wassermann reaction is found in many patients who present no clinical signs or symptoms, or whose symptoms are so equivocal that a clinical diagnosis of syphilis cannot be made.

500 such cases giving a positive Wassermann reaction have been subjected to searching examination and analysis; they may be divided in the first place into:

A. **Latent** syphilis proper, 28 per cent.: in this condition careful examination fails to reveal any clinical signs or symptoms of syphilis.

B. **Occult** syphilis, 72 per cent.: in these cases there are signs or symptoms of a general character, not pathognomonic of syphilis, which may nevertheless be shown to be of syphilitic origin. The final proof that some trivial or equivocal symptom is due to occult syphilis lies in its cure by antiluetic treatment; but the author claims, and presumably with justice, that work in a clinic in which the Wassermann test is done as a routine sharpens the physician's powers of observation; while comparison of numbers of cases of occult syphilis gives him a more extensive and accurate knowledge of its symptomatology. These non-pathognomonic signs and symptoms are:

I. General constitutional.

(1) **Pallor.** An ashy-grey complexion, frequently with a brownish leathery tinge, is characteristic. It is noteworthy that many patients showing this pallor have a normal blood count and haemoglobin-content; in these cases the pallor must be due to lack of blood in the superficial capillaries, possibly caused by a toxic action on the vasomotor nerves.

(2) **Loss of weight.** Observed in one-third of the total number of cases. Sometimes extreme, frequently as much as 30 or 40 lb. The specific origin of this derangement of metabolism is demonstrated by the immediate gain in weight following antisyphilitic treatment.

II. Changes in the blood.

(1) **Diminution of erythrocyte count.** In about 200 cases the red corpuscles were normal in number; in the remaining 300 there was anaemia. Red corpuscles and haemoglobin were generally diminished in the same proportion, the Hb-index remaining approximately 1·00.

That this anaemia is syphilitic cannot ever be stated on clinical grounds alone, even when other obvious causes have been excluded. Nor does the presence of a positive Wassermann test prove it to be of syphilitic origin. Diagnosis is made therapeutically. While iron and arsenic have no effect, the result of mercury or salvarsan is magical. That the improvement is due to the spirochaetocidal action of salvarsan, and not to the direct effect of arsenic on the blood-forming elements, is shown by mercury producing the same effect.

(2) **Lymphocytosis.** Occurring as it does in many diseases, lymphocytosis also can only be shown to be syphilitic when it disappears under

specific treatment. The effect of treatment is illustrated by a chart of one case:

		Before Treatment.	Thirty days later, after three injections each of Hg and Salvarsan.
	Erythrocytes	4 million	5 million
	Haemoglobin	58 %	95 %
White cells	Polymorphs	49 %	70 %
	Lymphocytes	41 %	25 %

III. Central nervous system.

(1) **Sleeplessness.** Relatively greater difficulty in going to sleep, and shorter sleep than formerly. Nightmares, hypnotics do not relieve.

(2) **Headache.** Usually intermittent, coming on in the evening. Frequently severe. Variously situated.

Syphilis should always be borne in mind as a possible cause of a headache for which no organic cause can be discovered.

Three theories have been advanced for the pathology of syphilitic headache and insomnia: (*a*) periostitis of the cranial vault; (*b*) mild chronic meningitis (Altmann, Dreyfus, Frühwald); (*c*) Cerebral vascular disease (Nonne).

(3) **Psychical changes.** May conform to one of two types: (*a*) an 'irritable weakness' of neurasthenic type; (*b*) hysterical.

Neurasthenic symptoms were present in 60 cases, and hysterical in 25, out of the 500.

To the former type were referred patients complaining of the onset of lassitude following slight exertion, loss of power of concentration and mental effort, irritability of temper for inadequate reasons, depression, and the usual diverse neurasthenic somatic symptoms. No cases of major hysteria were observed in this series.

The association of psychoneurosis with syphilis has been abundantly discussed, especially by Charcot and his school and Kraepelin. The latter considered these neurasthenic symptoms as the earliest expression of cerebral syphilis; but it is hardly possible to establish an organic relationship with certainty. The psychological effect upon the patient of his knowledge that he is syphilitic must be a factor in producing mental depression.

Of diagnostic importance is the onset of hysterical or neurasthenic symptoms in a patient previously psychically normal. In such cases syphilis should be reviewed as a possible cause. A positive Wassermann reaction, in a suspected case, increases the probability of the diagnosis; and Nonne and others have shown that specific treatment, by effecting a cure, proves the causal relationship. The pathology of the condition may be either a direct poisoning of the cortical cells, or depressed cerebral metabolism consequent upon impoverished blood or enfeebled cerebral circulation.

IV. **Enlargement of the spleen.** Observed in 55 cases out of 500 (11 per cent.). In a few cases palpable. Doubtless directly toxic in origin.

Examination of the spleen should never be omitted in any case where occult syphilis may be suspected: for syphilis is certainly the commonest cause of splenic enlargement. Naturally other causes must be excluded: amongst others one of recent importance, viz. antityphoid inoculation, after which enlargement of the spleen may sometimes be observed persisting for some months. Accurate history-taking is essential in such cases.

V. **Cardio-vascular.** (1) **A systolic murmur** was present in 28 per cent. of the cases, chiefly those presenting anaemia or nervous symptoms. It should be regarded as only indirectly due to syphilis.

Functional heart disorders, such as have been described by Grassmann in secondary syphilis, were not observed in this series. No instance of aortic disease was discovered; 46 cases were X-rayed, but the aorta was of normal calibre in all.

(2) **Albuminuria** was present in 70 cases, in all degrees from a mere trace to a definite cloud on testing. Whether syphilis had any causal relationship was doubtful. The refractile lipoid casts and severe albuminuria, described by Munk as characteristic of renal syphilis, were not found in any cases.

VI. **Fever.** Important observations were made in this connexion. Syphilis is rarely suspected in considering the differential diagnosis of obscure febrile conditions. There is, however, no doubt that occult syphilis may cause fever, even in cases in which no organic disease can be demonstrated. Two types noticed were (*a*) moderate intermittent fever; (*b*) a large diurnal swing without any great rise above the normal.

Just as with anaemia, fever can only be diagnosed as of syphilitic origin by its response to treatment. In this way 60 cases (12 per cent.) were found to have fever due to syphilis, and were cured by appropriate treatment. It is interesting to find H. Kraus describe the cure by mercury of four cases of pyrexia, sent into his sanatorium diagnosed as tuberculosis; in these cases fever was the only sign of an occult syphilis.

The length of time elapsing between infection and the first appearance of symptoms of occult syphilis could not be determined exactly. In hospital out-patients both accurate histories and continued observation are lacking. Only 20 per cent. of the cases gave a definite history of syphilitic infection. Nevertheless it may be stated that the nervous symptoms occur fairly early, i. e., one to two years after infection. Pallor, loss of weight, and probably also anaemia, are later manifestations; they were occasionally seen as early as two or three years after the primary stage. In only 10 of the 60 cases of syphilitic pyrexia could a history of infection be obtained: in these from two to seven years elapsed before fever was observed. The less complete the treatment is in the early stages the earlier will symptoms of occult syphilis be observed in cases in which they occur.

Summary. Latent syphilis in the strict sense of the term presents no symptoms. It can only be diagnosed by a history of infection or a positive Wassermann test. Occult syphilis causes a number of symptoms indicating general bodily infection. The individual symptoms vary in diagnostic importance. Pallor and splenic enlargement are the most characteristic; anaemia, lymphocytosis, nervous disorders, and defective heat-regulation are found in many other diseases: if other causes can be excluded, syphilis may justifiably be suspected. A definite diagnosis can be made only when the Wassermann test fortifies the clinical suspicion, and antisyphilitic treatment cures the patient.

Friedländer describes a supposed case of **transmission of syphilis in the latent stage**. The patient was an insane youth of 18, with no clinical signs of present or past syphilis; the Wassermann reaction of his blood was negative, while that of the cerebrospinal fluid was positive in 0·1 dilution. He bit a male attendant in the hand; a sore resulted which resembled a primary chancre, but search for spirochaetes was omitted. Twenty-three days after having been bitten the attendant's blood gave a strongly positive

Wassermann. The attendant had not been examined for syphilis before the injury; he denied previous infection, and bore no marks of healed syphilitic lesions.

The case for transmission must be regarded as not proven in this instance, as there are too many unknown factors concerned.

Syphilis of the stomach. Bensaude and Rivet, after referring to the previous observations of Hayem and Lacapère, conclude that syphilis of the stomach is of comparatively frequent occurrence, and that many cases pass unrecognized owing to the fact that they subside in the course of the usual treatment for syphilis. The chief lesions are tertiary manifestations : gummatous infiltration, ulcerations, and hyperplastic infiltration with cicatrices leading to stenosis.

Syphilitic ulcer of the stomach presents the same symptoms as ordinary gastric ulcer. Haematemesis may be severe. Bensaude and Rivet report four cases, two of which were cured and two relieved by antisyphilitic treatment by hectine and mercury. They quote Castaigne who found frequent evidence of syphilis in men discharged from the army with the diagnosis of gastric ulcer. In the pseudo-cancerous form of syphilitic ulcer the presence of a tumour of variable size and position is added to the symptoms of gastric ulcer. An example is given in which pyloric infiltration with haematemesis and wasting of several years' duration was cured by antisyphilitic treatment. Sometimes there may be hybrid cases of syphilis and cancer, the latter being uninfluenced by specific treatment.

Hyperplastic infiltration may be limited to the pylorus or generalized. It is of slow progress and may cause stenosis of one orifice and shrinking of the stomach. A remarkable example is given of a woman aged 35, with no history of syphilis, who suffered from epigastric pain, vomiting and wasting. Radioscopic examination showed double stenosis—at the cardiac orifice and in the middle of the stomach. Oesophagoscopy showed an ulcer at the cardiac orifice. Under mercurial treatment the cardiac stenosis disappeared and the mesogastric stenosis improved. Radioscopy then showed a condition of pyloric incontinence with dilatation of the duodenum and a contracted stomach. This condition remained permanent, but the patient regained good health.

Syphilitic stenosis of the pylorus may be of slow progress or rapid, simulating cancer. An illustrative case occurred in a man aged 63, who suffered from abdominal pain and wasting for five years. A hard tumour was felt at the pylorus, and radioscopy showed pyloric obstruction. The Wassermann reaction was positive. There was a history of syphilis 42 years ago. The symptoms and tumour disappeared under treatment by hectine and mercury. In other cases, owing to fibrous tissue formation, gastro-enterostomy may be necessary.

Bensaude and Rivet remark in conclusion that gastric syphilis is characterized by polymorphism and has no pathognomonic signs of its own. It must be diagnosed by the history, the presence of other signs of syphilis, the Wassermann reaction, the chemistry of the stomach contents, and by radioscopy. Multiple lesions and an irregular X-ray picture suggest syphilis. The therapeutic test, by salvarsan or mercury, should give a rapid result. Mercury and iodides are well borne by the mouth in gastric syphilis, but not in non-syphilitic cases. Improvement in symptoms and gain in weight are rapid. Cases with stenosis are less amenable to treatment and may require surgical intervention.

Milian (1) (2) reports three cases of **icterus** occurring in secondary syphilis during arsenical treatment. He considers these of syphilitic origin, since the icterus cleared up under treatment with intravenous injections of cyanide of mercury, after which larger doses of arsenobenzol were given without any recurrence of the icterus. In one case the icterus was cured by oral administration of mercury, which, as he remarks, is the best route to the liver. He denies the existence of arsenical icterus, and holds that late icterus is also of syphilitic origin, that it comes in the same category as 'neuro-recurrences', and is due to hepatic syphilis awakened by insufficient treatment. Other cases he explains by coincident catarrhal icterus.

The subject of **syphilitic and arsenical jaundice** is discussed by Scott and Pearson in a preliminary report from the Canadian Special Hospital in England. They divide the cases into two groups; first, those occurring in untreated syphilis and due to invasion of the liver by the *T. pallidum*; second, those occurring during or subsequent to salvarsan treatment, which may be due to the disease, the drug, or a combination of both. The incidence of the first group is small; only two cases occurring in 2,243 patients treated at the above hospital. In this group the jaundice is due to diffuse degeneration of the liver cells produced by the toxic action of the *T. pallidum*. The incidence of the second group is greater, 39 in the 2,243 patients treated with various arsenical preparations. In this group, according to Scott and Pearson, the jaundice is due to the toxic action of arsenic superimposed on syphilitic degeneration of the liver cells, and not an obstructive jaundice. They advise that every case of syphilis should be carefully examined for any previous or present condition that would cause damage to the liver, and that when this is found great care should be exercised in treatment. When jaundice appears they recommend immediate suspension of arsenical treatment, rest in bed, milk diet, free catharsis and an intramuscular injection of 3 c.c. of intramine repeated three days later and followed by a further injection of 5 c.c. a week later. They regard intramine as a specific for early and late combined syphilitic and arsenical jaundice, and also as apparently a specific against the toxic action of the arsenical compounds, especially on the liver. The patient should receive no further antisyphilitic treatment for a month, and no further arsenical treatment for at least a year. Treatment, in such cases, should be carried on with mercury and iodide.

Morris reviews our knowledge of **syphilis of the lungs.** It is a striking fact that this disease so seldom attacks the lungs, for out of 2,800 autopsies performed at the Johns Hopkins Hospital Osler reports only 12 cases, and 8 of these were of the congenital type. Morris points out that the gummatous form of congenital syphilis of the lungs is rare, whilst 'white pneumonia' and 'interstitial pneumonia' are much more common. These two latter lesions are generally combined. In 'white pneumonia' the lungs are abnormally large and are marked by impressions of the ribs. The organ is of a greyish-white colour, is dry, and the alveoli and the smaller bronchi are filled with masses of cells. By reason of the pressure of this exudation of cells, the blood-supply to the lung is greatly impoverished. In the case of 'interstitial pneumonia', as the term implies, there is extensive infiltration by small round cells of the interlobular connective tissue and the tissues about the bronchi and blood-vessels. This change may readily be made out with the naked eye. Also the intima of the small arteries is thickened. Children born with congenital syphilis of the lungs do not live long. It is to be regretted that Morris did not discuss the question of the liability of congenital syphilitics to attacks of lobar pneumonia.

Syphilis of the lung may also be of the **acquired form**; (1) **Gummata** are prone to occur close to the hilum and may be of any size up to that of a hen's egg. Usually cicatricial tissue forms at the site of a gumma and contraction of the lung follows; but more rarely a gumma ruptures into a bronchus forming a cavity in the lung. (2) **Bronchopneumonia** may show itself in syphilis of the lungs in small patches of consolidation with healthy tissue between. (3) **Fibroid induration** or chronic interstitial pneumonia may occur. As in the congenital type, the changes are chiefly about the bronchi and blood-vessels, but sometimes very widespread patches of sclerosis may be found in one lobe or even throughout a whole lung. (4) **Syphilitic phthisis,** according to Morris, is the rarest manifestation of pulmonary syphilis and results from a caseous gumma emptying into a bronchus. It is a condition very readily confused with tuberculosis, and Fowler has laid down strict rules as guides in differential diagnosis. It must be shown that definite syphilitic lesions are present elsewhere in the body and that there is no tuberculosis of the lungs. Only a post-mortem examination can prove the latter fact. The symptoms and physical signs of pulmonary syphilis are not pathognomonic. The diagnosis is made by excluding tuberculosis. In contrast with tuberculosis, syphilis often begins at the root of the lung and does not progress in any well-defined direction.

Cavity formation is rare in the case of gumma of the lungs and is the rule in caseous tubercle. Stenosis of the trachea or of a main bronchus may occur in syphilis, and any cavities that may arise are generally bronchiectatic and not due to progressive destruction of the lung as in tuberculosis. Pulmonary aneurysms are rare in syphilis of the lung. Lesions of the lung are very infrequent in syphilis. Syphilis may so undermine the resistance of the patient that tuberculosis attacks him, and indeed both diseases may be present in the lungs at the same time.

Congenital syphilis of the endocrine glands. In an interesting article Barthélemy discusses the part played by disease of the endocrine glands due to congenital syphilis. He points out that all these glands are at the mercy of hereditary syphilis, and that it is logical to conclude that the dystrophic effects so common in the hereditary disease are the result of a disturbance of the trophic regulatory system caused by disease of these glands. Affections of all the endocrine glands have been reported in hereditary syphilis by several authors; in the pancreas, suprarenals, thyroid, hypophysis and ovary. The *T. pallidum* has been found everywhere, with or without histological lesions, often in masses; but actual lesions are more common. These may be in the form of miliary gummas, larger gummas, gummatous infiltration or sclerosis, the last being most frequent. A case was reported by Triboulet concerning an heredo-syphilitic infant a month old which died suddenly. At the autopsy lesions were found in the suprarenals, thyroid and parathyroids, and hypophysis. Numerous specimens of *T. pallidum* were present in all the lesions.

Other cases, in which there was clinical evidence of affection of the endocrine glands in heredo-syphilitics and in which improvement took place after antisyphilitic treatment combined with opotherapy, have been reported.

Thus Hutinel recorded the case of a child aged 7 years, suffering from heredo-syphilitic disease of the bones and skin with severe cachexia which was improved by opotherapy and injections of benzoate of mercury. Costa reported the case of a young soldier affected with multiple glandular disorders causing eunuchoid gigantism, acromegaly, hypothyroidism, vasomotor troubles of the extremities, suprarenal insufficiency with pigmentation and hypotension. Improvement took place in this case after mercurial treatment alone. Clark reported a case of exophthalmic goitre in a woman of 24 presenting signs of heredo-syphilis (natiform skull, epileptic attacks, and positive Wassermann reaction) who was cured after three months' treatment with salvarsan. In a case of T. Barthélemy's, a heredo-syphilitic woman with hypothyroidism and polyarticular rheumatism was cured by mercury and iodide of potassium.

Schulte and Lemonnier cured two cases of diabetes mellitus in heredo-syphilitics by specific treatment. Such observations are convincing because they show the result of antisyphilitic treatment, but there are other cases where in the absence of this result, evidence of syphilis can be obtained by the history, presence of stigmata, and a positive Wassermann reaction. For example, two cases reported by Pel where an acromegalic brother and a myxoedematous sister, with a healthy brother, were the only survivors of nine pregnancies, the father having contracted syphilis two years before marriage. E. Fournier collected numerous cases of infantilism, dwarfism and giantism in which there was evidence of heredo-syphilis. Other cases of multiglandular affections, osseous dystrophy, obesity, &c., occurring in the subjects of heredo-syphilis have been improved by combined opotherapy and antisyphilitic treatment. Such treatment should be commenced early, for the endocrine glands are affected at an early period, often in intrauterine life, as shown by autopsies on the foetus.

Barthélemy is of opinion that the effects of endocrinal syphilis such as dwarfism, infantilism and myxoedema may reach the third generation.

Marfan holds that **rickets** may be produced by all infections and chronic intoxications occurring in the active period of ossification, a period which extends from the last months of intrauterine life to 18 years. But it is especially in the last months of intrauterine life and up to the end of the second year that infections and intoxications determine rickets. At all periods the most frequent cause of rickets is congenital syphilis. Next in frequency come tuberculosis and digestive disturbances. Congenital syphilis may give rise to two kinds of lesions in the bones of the infant: (1) syphilitic osteochondritis; (2) changes apparently non-specific which may be produced by other causes. Both kinds of lesions may occur alone or in conjunction. Syphilitic rickets is characterized by four characters; (1) early onset, during the first three or four months of life; (2) predominance of cranial lesions—cranio-tabes, natiform skull, dilatation of subcutaneous veins of the head; (3) pronounced anaemia; (4) chronic hypertrophy of the spleen; this is common in congenital syphilis with or without rickets, but, according to Marfan, it is always syphilitic when occurring in the first three months.

The changes in the blood in secondary syphilis were investigated by Fischer and Chen Pan Nien in sixteen cases. To compensate for the small number of cases, numerous observations were made on each case, in order to eliminate accidental variations. The following conclusions were reached:

In secondary syphilis there is practically invariably a small diminution in the erythrocyte count (average 4,270,000 per c.c.) The haemoglobin-content of the blood falls in the same ratio (to an average of 85 per cent.); the Hb-index remains approximately 1·00. The white cells are slightly increased in number, the average being about the upper limit of the normal. There is a small but appreciable reduction in the percentage of polymorphonuclear leucocytes, accompanied by a corresponding increase of the small mononuclear cells. Taken in conjunction with the relatively high white-cell count, this implies that there is a moderate but quite definite lymphocytosis, not only relative but absolute. The percentages of polymorphs and lymphocytes averaged 60 per cent. and 30 per cent. respectively.

The pathological changes are thus comparatively slight in degree, but definite.

The authors considered the observations insufficient to determine whether these changes were due to syphilis or the result of treatment, but incline to the view that they are due to the disease. They were unable to assert from their observations that any appreciable alteration occurred in the average blood count during the course of treatment. Their figures warrant the conclusion that a single examination of the blood of any individual case has practically no diagnostic value in suspected syphilis.

Nicolau, examining the **cerebrospinal fluid** in 51 cases of primary syphilis, found lymphocytosis in 18. In these there was pure lymphocytosis in 13, lymphocytes and endothelial cells in 4, and in one case the addition of plasma-cells. The meningeal reaction in primary syphilis is in most cases slight and does not appear till the third week. Nicolau remarks that inequality of the pupils was found in 11 out of the 18 cases.

Diagnosis. The importance of demonstrating the *T. pallidum* in early primary syphilis when the serum reaction is negative, a time when abortive treatment by salvarsan and mercury is most likely to be successful, is emphasized by Hoffmann. He does not agree with Wassermann's distinction of sero-negative primary syphilis as a blood spirochaetosis like relapsing fever and sero-positive primary syphilis as a tissue infection. As he showed in 1905, the *T. pallidum* is from the first a tissue infection which can only be influenced by prolonged treatment. The same applies to the glandular enlargements, which develop immediately afterwards. The Wassermann reaction generally becomes positive in the fifth or sixth week after infection, but may be delayed till after the roseola. Indeed, in rare cases there may be sero-negative secondary syphilis which by weekly tests show no change to positive. Hoffmann mentions a case of this kind, with iritis and syphilitic angina, which remained negative for a year. Hence it is impossible to make a sharp distinction between sero-negative and sero-positive primary syphilis. Hoffmann is also of opinion that an abortive cure may be realized in sero-positive primary syphilis with intensive salvarsan and mercury treatment, administered in two courses of 8 to 10 weeks.

Hoffmann is of opinion that if material is properly obtained from the primary sore and the regional glands an early diagnosis is nearly always successful. Care must be taken not to mistake 'pseudo-pallida' for true *T. pallidum*. This applies not only to the spirochaetes of the buccal cavity, but also to those of the genital organs, where finer forms of the *S. refringens* and the spirochaetes of balanitis may often resemble *T. pallidum*. When material is obtained from the surface, after cleansing with normal saline, Hoffmann's rule is that the *T. pallidum* should only be diagnosed when it has at least 8 to 10 very thin, steep, and corkscrew spirals, and when no other irregular or larger forms of spirochaetes are present. The best way to avoid error is to obtain material by puncture of the chancre and glands, by which means, according to Hoffmann, the *T. pallidum* can be found in 90 per cent. of cases at the first examination. Hoffmann warns against diagnosis made from material obtained by unskilled practitioners; also against specimens forwarded in the form of dried smears or in capillary tubes filled with secretion, in which the *T. pallidum* may assume irregular forms. He points out the importance of making a Wassermann test in all cases of soft chancre or doubtful venereal sore; for a negative reaction which becomes positive later will show a fresh infection, while a positive reaction will show the presence of former syphilitic infection.

Pick states that the importance of an X-ray examination in suspected cases of congenital syphilis lies in the fact that the bony changes are (1) constant and (2) specific. Minor advantages are the rapidity and convenience of the process.

Apart from simple gummata, the bony changes in the syphilitic infant or foetus comprise (1) osteochondritis and (2) ossifying periostitis.

Wegner has described osteochondritis as occurring in three objective stages, namely:

i. Increased breadth of zone of provisional calcification; the zone presents an irregular jagged border directed towards the growing edge of the epiphyseal cartilage.

ii. (*a*) Further widening of above zone, which now appears as a yellowish-white band on section, often definitely granular.

(*b*) The normal production of bone spicules on the diaphyseal side is reduced to a minimum; instead a layer of calcified cartilage extends deeply into the diaphysis (the 'chalk-lattice-work' of B. Schmidt).

iii. A layer of granulation-tissue appears immediately next to the 'chalk-lattice': it is prone to necrosis and softening, and is indeed regarded by many workers as essentially gummatous material. This granulation layer is often double, with a band of 'chalk-lattice' separating the two portions. If it extends throughout the diameter of the bone, a solution of firm continuity is produced, forming the so-called 'separation of epiphysis'. In many cases, however, it has been shown that there occurs a real fracture of the fragile bone-spicule layer, the two portions being held together by periosteum without blood-effusion.

In X-ray plates, the first stage shows a broad band, corresponding to the zone of provisional calcification, which is jagged on its epiphyseal side; the second stage shows similar appearances, more defined: in the third stage the layer of granulation tissue appears as a cloudy or clear band, which is characteristically double or even triple.

These appearances are seen most often at the lower and upper ends of the femur; but all the long bones present the same changes in a fairly definite order of frequency. The clavicle and phalanges are not exempt. The same lesions may be seen in the borders of the scapula; at the crest of the ilium, and the pubic and ischial angles of the os innominatum: also in the vertebrae, sternum, and ribs.

As a means of differential diagnosis between congenital syphilis and rickets, infantile scurvy or tubercle, X-ray examination is unequalled. It is also the best method to apply to dead foetuses and still-born infants: a special advantage is that artefacts are avoided.

Ossifying periostitis is rendered obvious by X-rays in the long bones and ribs, in a fashion which is not demonstrable with certainty by anatomical means, nor easily so by histological methods.

Prophylaxis. Much of the evidence in favour of immediate prophylaxis, or self-disinfection, in case of exposure to possible venereal contagion has, so far, been unpublished, but several articles have appeared recently in which the case for immediate prophylaxis receives strong support. Sir James Barrett, describing the management of venereal diseases in Egypt during the war, states that in his own unit, the 1st Australian General Hospital, prophylactic outfits of calomel ointment and argyrol jelly were issued to those who applied for them, and that of all the men who were supplied with these outfits only one became infected, and he had not used it.

Sir Archdall Reid, when in charge of a rapidly changing body of men, averaging 2,000, at a seaport town, found that venereal disease was common among them in spite of moral lectures and so-called 'early treatment' after return to quarters. He, therefore, instituted immediate self-disinfection, each man who applied being given an ounce of a 1 in 1,000 solution of potassium permanganate and a swab of cotton-wool with careful directions how to use them. During 1917 and 1918 about 20,000 men passed through the station, and only seven cases of venereal disease occurred, one of syphilis and six of gonorrhoea. Of the latter, two cases were contracted by men on leave, from their wives; two others were drunk, and one did not use the solution. The man who contracted syphilis had a long prepuce and did not apply the solution till two hours after intercourse.

Surgeon Commander P. H. Boyden had equally good results with the same solution in the navy. During a period of nine months not a single case of gonorrhoea occurred among those who used this method, and only one of syphilis, and in this case the solution was not used till six hours after exposure to infection. The number of officers and men under his care was 2,000. Both Sir Archdall Reid and Surgeon Commander Boyden consider that there is no special virtue in potassium permanganate and that any other active antiseptic would be equally effective; but permanganate is the cheapest, the least poisonous, and the least irritating.

Miss Ettie Rout, writing on the prevention of venereal disease among the Anzac troops, states that in August and September 1917 over 5,000 troops came on leave to Paris; no disinfectants were issued and 20 per cent. became infected: whereas, from November 1917 to March 1918 over 30,000 troops came on leave, disinfectants were freely issued, and only 3 per cent. became infected.

Schereschewsky states that an ointment of quinine is a good prophylactic against syphilitic infection. In a German camp much exposed to venereal infections those who applied this ointment are said to have escaped. He refers to some former experiments of his on apes, in which he claims to have proved that the application of quinine ointment within five hours after inoculation with syphilitic material prevented the development of syphilis. Unfortunately, the composition of the ointment is not stated.

Treatment. Gennerich reports favourably on **silver-salvarsan.** He uses doses of 0·1 to 0·3 gm. dissolved in 20 to 30 c.c. of 0·4 per cent. salt solution, administered by means of a syringe. The injection should be slow (5 to 7 minutes); otherwise, angio-neurotic symptoms such as swelling of the face, cyanosis, &c., may arise. The intervals between the injections should be 4 or 5 days. In sero-negative primary syphilis he gives 5 to 6 injections; in sero-positive primary syphilis 7 to 10; in secondary syphilis 8 to 12. Compared with salvarsan, the side effects were slight; out of 1,000 injections there were only four cases of fever, slight dermatitis, and icterus. The appearance of erythematous swelling of the face is an indication for suspension of treatment, otherwise severe dermatitis may arise. The preparation is said to be well borne by young individuals, but in older subjects and in women the dose should not exceed 0·2 gm.

Goldberger points out that histological research shows that silver has a special affinity for spirochaetes. He recommends combined treatment with silver-salvarsan and mercury.

Schonfeld and Birnbaum conclude that **silver-salvarsan** has a rapid effect on the clinical symptoms of syphilis and also on the glandular enlargements; that it is superior in action to neosalvarsan and sodium-salvarsan, but not quite as active as the old salvarsan though much less toxic. With regard to its effect on the Wassermann reaction, they found that in primary syphilis with a positive reaction two-thirds of the cases became negative in six weeks, but generalized secondary syphilis with a positive reaction was refractory after 11 or 12 injections in the course of 8 to 12 weeks. With regard to side effects, they found that the angio-neurotic symptom-complex was more frequent than with neosalvarsan and old salvarsan, but permanent damage was not observed. In older cases of syphilis combined treatment with mercury is recommended.

Hoffmann recommends an intensive combined treatment with mercury and sodium-salvarsan or neosalvarsan (8 to 10 injections) at the earliest sero-negative stage of primary syphilis, with a view to attain complete sterilization. In secondary syphilis, he regards salvarsan alone without mercury as dangerous, on account of 'neuro-relapses'. He mentions four cases in which these occurred, and states that by combined treatment with mercury they may be avoided. The mercurial treatment he recommends is either by inunction or injections of mercury salicylate. Hoffmann concludes that abortive treatment, by this strong combination of mercury and salvarsan, is usually successful in sero-negative primary syphilis, and frequently so in sero-positive primary syphilis. In early secondary syphilis, in the majority of cases, it leads to early healing, prevents neuro-recurrences, and also the highly contagious relapsing lesions.

Copelli has investigated the effect on syphilis of the organic compounds of vanadium, phosphorus, arsenic, and antimony prepared by Bocchi. These different preparations were first tried on the rabbit by intravenous and intramuscular injection to determine the toxicity. The preparations of vanadium were the most toxic. By intravenous injection the minimum lethal dose was 0·20 gm. per kilo for vanadium; 0·60 gm. for phosphorus; 0·70 gm. for arsenic; 0·80 gm. for antimony, and 1 gm. for the compound containing vanadium, arsenic, and antimony. As regards the parasiticidal action of the drugs *in vitro*, they had no action on the *T. pallidum*, nor on cultures of enteric, anthrax, pyocyaneus, streptococci, or staphylococci. The therapeutic action was then tried on rabbits inoculated with syphilis. In the control animals the experimental chancre developed between the 40th and 80th day. In the animals treated with the different compounds, the chancre healed after 0·05 gm. of vanadium per kilo, after 0·50 gm. of phosphorus, after 0·60 gm. of arsenic, and after 0·30 gm. of the combination of vanadium, arsenic, and antimony. The author thinks that these compounds have a parasitotropic action on the *T. pallidum in vivo*, although none *in vitro*. Finally, after intravenous injection of a combination of vanadium, arsenic, antimony, and phosphorus the experimental chancre of rabbits was cured with a dose of 0·20 gm. per kilo. Hence the author concludes that the association of these different substances increases the action of each of them.

Linser advocates the simultaneous intravenous injection of **neo-salvarsan** and **perchloride of mercury**, in doses of 0·45 gm. of the former and 0·02 gm. of the latter, administered twice a week. The perchloride was used in a 1 per. cent. solution without the addition of sodium chloride. Both drugs were dissolved in warm water and injected with a glass syringe. Good results are claimed from this combination after an experience with about 8,000 injections given to 1,000 patients.

Treatment of cerebrospinal syphilis. In the treatment of syphilis of the central nervous system, Nicholson uses intraspinal injections of **combined mercurialized serum and salvarsanized serum.** The technique is as follows: a donor of blood is selected, either normal or a syphilitic with a negative Wassermann reaction after sufficient treatment. Under aseptic precautions, 500 c.c. of blood are withdrawn into a sterile flask, allowed to clot, and placed in the ice-box overnight. The next morning the serum is pipetted off into several 50 c.c. centrifuge tubes, centrifugalized for half an hour and stored in dark bottles. Into some of these are put 15 c.c. of the serum; they are then placed in a water bath at 56° C. for half an hour to destroy complement and inhibitory substances in the serum. The corks are then paraffined and the bottles placed in the ice-chest. Into other bottles 1 c.c. of a solution of perchloride of mercury in sterile water is placed, some containing 1/50 grain and some 1/100 grain of the salt. To each bottle containing the mercury solution 12 c.c. of the centrifugalized serum are added, at first drop by drop, and well shaken after each drop to avoid accumulation of the undissolved albuminate of mercury. The total quantity is made up to 30 c.c. by the addition of sterile normal saline solution, heated to 56° C. for half an hour in a water bath, sealed with paraffin, and placed in the ice-box. The mercurialized serum is now ready for use after warming to body temperature, and will keep indefinitely. Sterile human serum is also ready in other bottles for the addition of 0·5 mg. of salvarsan on the day of administration. After this addition the mixture must be incubated for two hours at 37·5° C. and heated a second time to 56° C. for 20 minutes. The sterile serum is considered fit for use so long as there is no sediment after agitating the bottle, and can be kept for some weeks as a stock serum. Nicholson has abandoned the Swift-Ellis method of salvarsanized serum *in vivo*, and replaced it by the above combination of mercurialized serum and serum salvarsanized *in vitro*—a combination of Byrne's and Ogilvie's methods. The best results were obtained in interstitial cerebral syphilis, including gummata and meningitis. Improvement took place also in cases of tabes. In four cases of general paralysis, however, the treatment failed. In these cases, Nicholson remarks, the treatment may have precipitated more grave symptoms. The most deceptive feature of these cases, he says, is apparent improvement immediately after treatment which may last several months, but this improvement in his cases proved to be only the calm before the storm. In conclusion he emphasizes the importance of giving general systemic treatment in combination with intraspinal therapy.

Sicard, Haguenau, and Kudelski recommend small daily doses of the **arsenical preparations** in the treatment of cerebrospinal syphilis. The preparations they used were novarsenobenzol, sanar, and galyl, in doses of 0·15 c.gm. up to a total of 6 to 7 gm. for a woman and 7 to 9 gm. for a man, the total number of injections being from 40 to 60. No mercury was given. By this method they claim that severe reactions such as 'nitritoid crises' and 'serous apoplexy' are avoided. 'If these reactions are due to anaphylactic shock', they remark, 'we can understand that daily injections may neutralize the period of anaphylactic incubation and produce tolerance.' The other side effects of the drugs which they noted were erythema, absence of ankle-jerk, icterus, and variations in weight and temperature. Early erythema occurred in 10 per cent. of the cases and was transient, disappearing after cessation of treatment. Late erythema, occurring at the end of the course of treatment, is more serious and is a sign to stop treatment; otherwise severe dermatitis may follow with loss of hair, onychia, keratodermia, bullae, and ulceration of the skin. Bilateral absence of the ankle-jerk was common after 6 to 10 injections, and was very persistent. The authors regard this sign as an indication to stop treatment; otherwise paresis may ensue. Icterus was observed five times in more than 100 cases. One case developed at the end of treatment, the others between the fourth and eighth week after cessation of treatment. The first case was fatal, but the patient was in an advanced stage of general paralysis. The other four cases recovered. In two of those cases—one of hemiplegia in a woman of 50, the other one of multiple sclerosis—there was no evidence of syphilis and the Wassermann reaction was negative both in the blood and cerebrospinal fluid. In these cases, at any rate, the icterus must be attributed to arsenic. The authors draw attention to the importance of the estimation of urea in the blood in the course of arsenical treatment, since the affinity of arsenic for the hepatic cells disturbs the uropoietic function of the liver and appears to cause a progressive hyperazotaemia which continues some time after cessation of treatment.

In a paper entitled, 'Has Salvarsan a toxic action on the Optic and Auditory Nerves?' Zeissl says he judges from his experience of 4,000 injections of Ehrlich's salvarsan, and that he has collaborated with aural specialists in all doubtful cases of deafness. He has not seen a case of auditory or optic nerve trouble which was indubitably due to salvarsan. Cranial nerve lesions are caused by syphilis, and not by salvarsan, he thinks: and he cites with approval Lesser's dictum, that such nerve lesions in syphilis are due to the pressure of cranial periostitis or pachymeningitis. The author's flat denial of his belief in the Jarisch-Herxheimer reaction will discount his evidence for many readers. A case of double cochlear-nerve disease in the tertiary stage, cured by salvarsan, is described; four other cases mentioned are interesting, but not conclusive. Optic neuritis is not discussed.

Deaths after salvarsan. Herzog reports three cases. In the first case, a girl of 19, death occurred after three injections of salvarsan. At the autopsy numerous punctiform haemorrhages and small foci of softening were found, chiefly at the base of the brain and in the central ganglia. In the second case, a woman of 26, similar changes were found in both hemispheres and in the central ganglia. Microscopic examination of both these cases showed numerous thrombi in the small vessels and capillaries with consequent extravasation of blood and foci of softening. In the second case these foci were found at various levels in the spinal cord. In the third case, symptoms of encephalitis occurred two days after a single injection of neosalvarsan, together with paralysis and sensory disturbances in the legs. At the autopsy foci of softening were found in the spinal cord. Herzog draws attention to the inflammatory nature of the lesions and remarks on the importance of ascertaining whether these lesions have been known to occur after salvarsan treatment of non-syphilitic cases such as malaria and recurrent fever, in view of the theory that the *T. pallidum* or its toxins are the cause of encephalitis haemorrhagica. He makes no reference, however, to Mentberger's statement that haemorrhagic encephalitis has been known to occur after salvarsan treatment of non-syphilitic cases such as pernicious anaemia, and also after experimental injection in animals (*Die Arsentherapie der Syphilis*, 1913).

Blanton, reporting four fatalities following the administration of salvarsan, remarks that our knowledge concerning the toxicity of salvarsan and other organic preparations of arsenic is incomplete, and that the severe reactions which are sometimes associated with their use are difficult to classify, with the exception of the definite group known as haemorrhagic encephalitis. The reactions may be classified as follows: (1) Anaphylactoid, appearing during administration of the drug, lasting 15 to 30 minutes and characterized by flushing and oedema of the face, injection of mucous membranes, nausea, vomiting, and a sense of suffocation, sometimes pallor and unconsciousness. These cases are rarely fatal. The anaphylactic nature of this reaction has been investigated by Swift in experiments on guinea-pigs, and he believes that the patient's serum may be sensitized by salvarsan, and so changed that it acts like a foreign protein which is responsible for the reaction. (2) Deferred reactions appearing several hours after administration, lasting 12 to 24 hours, and characterized by headache, vertigo, nausea, vomiting, diarrhoea, fever, general pains, and sometimes skin eruptions. (3) Late reactions, appearing after 24 hours, often not till the second or third day, and characterized by vomiting, diarrhœa, and fever, followed by twitching of muscles, dilated pupils, absence of reflexes, and coma. Most fatal cases belong to this group. (4) Other reactions include (i) Herxheimer's reaction, said to be due to liberation of endotoxins or to insufficient dosage; (ii) so-called neuro-recurrences chiefly affecting the cranial nerves, and said to be due to a revival of pre-existing lesions: (iii) morbilliform skin eruptions, jaundice, and albuminuria. The explanations brought forward for these phenomena include disregard for contra-indications (cardio-vascular disease, advanced tertiary syphilis, nephritis, &c.) or administration in critical conditions, idiosyncrasy, over-dosage, failure to use sterile water, too hot or too cold solutions, too great or too small a volume of solution, too acid solution, too rapid administration, food or exercise before or after administration. Shamberg, Kolmer, and others have pointed out that the drug itself is probably the most important factor, and Shamberg has shown that these reactions are probably due to impurities in the drug, unidentified by-products. As salvarsan, &c., are not pure chemical compounds, different samples may vary and some contain impurities which cause the toxic phenomena. The four cases reported by Blanton belong to the third group, of late reactions. All followed an intensive course of 4 to 6 intravenous injections of salvarsan; the average interval between the injections being 4 days; the dose being from 0·4 to

0·6 gm. The intervals between the last injection and the onset of reaction was 2 days in three cases and 3 days in the fourth. Death occurred in 2 days in three cases and in one day in the other. The symptoms and post-mortem findings were similar in all cases—sudden and profound coma without cranial nerve paralysis. Two cases had convulsions. Cheyne-Stokes breathing was present in all cases, and death was due to failure of the respiratory centre. The brains in all cases showed minute haemorrhages confined to the basal nuclei and the walls of the lateral ventricles, cerebral congestion, and oedema. In one case there was fatty degeneration of the liver. All these cases occurred in healthy young men at the same time, and can only be explained by the presence of toxic by-products in the salvarsan.

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THE NERVOUS LESION OF BERI-BERI AND ITS BEARING ON THE NATURE AND CAUSE OF THE DISEASE

Great interest attaches at the present moment to the problem of the deficiency diseases, and very definite views have gained acceptance as to the nature and cause of certain of them. It may be a salutary exercise, therefore, to review the pathology and symptomatology of such a disease as beri-beri and to ascertain to what extent they are compatible with current hypotheses of their origin.

In the recent 'Report on the present state of knowledge concerning accessory food factors (vitamines)', compiled by a Committee appointed jointly by the Lister Institute and the Medical Research Committee, beri-beri is described as a severe form of peripheral neuritis caused by the absence from the diet of an essential accessory factor (p. 25). Few could now be found to dispute this general statement, though all must recognize that it is by no means a complete explanation of the origin of beri-beri. Perhaps, also, it fails to convey an adequate idea of how much yet remains unknown of the cause and nature of the disease. For example, we are still ignorant of the mechanism by which this specific dietary defect gives rise to beri-beri, and of how it is that starved fowls outlive the incubation period of the experimental form of the disease in appropriately fed birds, but die without developing it (Fraser and Stanton). Yet starvation is surely a state of vitamine deprivation. This passing mention of but two of the most obvious problems awaiting solution—one might almost say awaiting recognition—will serve to show how much is left unexpressed by the definition quoted, how much indeed, cannot be expressed.

Nevertheless, certain conclusions are implied in the theory which includes this definition, and these we may examine in the light of the clinical and pathological facts of the disease. It will be recalled that the deficiency hypothesis has replaced two main views of the origin of beri-beri. These are the infective and the intoxication theories. Further, the deficiency theory is in many important respects a new departure in pathology. As the report from which we have already quoted states (pp. 2–3), 'It is difficult to implant the idea of disease as due to deficiency. Disease is so generally associated with positive agents . . . that the thought of the pathologist turns naturally to such positive associations and seems to believe with difficulty in causation prefixed by a *minus* sign. . . . Even when Eijkman, through his admirable studies, had clearly established more than twenty years ago that beri-beri arose during the consumption of decorticated rice (making it clear, therefore, that something in the cortex was necessary to normal nutrition) he was led to suggest, not the simple view that the cortical substance was of direct use to the body, but rather that it was necessary to neutralize the otherwise deleterious effect of a diet over-rich in starch. Save for the mental bias just referred to it is very difficult to see why so roundabout an explanation should have been thought necessary.'

Now Vedder, in 1913, did actually go to the length advocated by the writers of this report and expressed the opinion that the 'anti-neuritic' vitamine is directly concerned in the nutrition of the nervous system, of which it is 'an essential building stone'. When a diet lacks this, the nutrition of the nervous system at once suffers and it degenerates until a point is reached at which the symptoms of beri-beri appear. It would thus seem that beri-beri is a slowly progressive degeneration of the entire nervous system. Similarly, in the infantile form of the disease, a consistent deprivation during foetal life and after birth of some substance 'essential for the growth and development of the child's nerves' (Andrews) is the underlying cause.

The neuropathologist, in considering the general principle thus enunciated in the 'Report' and expressed in the conclusions of Vedder, will at once detect therein the seeds of a dangerous fallacy. For Eijkman, who surely possessed the fundamental knowledge that primarily beri-beri is a polyneuritis indistinguishable both clinically and pathologically from the known forms of toxic polyneuritis produced by alcohol and diphtheria, was arguing very soundly when he came to the conclusion he did, and which, indeed, he still holds. How could he have justly reasoned that a symptomatology and a morbid anatomy resembling those of an intoxication, and in the production of which he was unable to exclude this cause, were due to a pathological process for which he had no analogy and no evidence, namely, a starvation degeneration of the entire nervous system?

Moreover, to the neurologist at least, the conception of positive and negative or 'minus' signs in the causation of disease phenomena is no new thing; it is not less than fifty years old. Since its formulation by Hughlings Jackson, this conception has profoundly influenced neurological thought in this country, and it is in virtue of this very principle that we cannot readily accept the view that beri-beri has solely a negative or 'minus' cause. In fact, the argument in its application to beri-beri may well prove a boomerang in the hands of the biochemist. For we cannot pass judgement on a disease in the laboratory in this manner without a careful scrutiny of all its features, clinical and pathological.

Speaking of cerebral disease, Jackson pointed out that *negative lesions* could not produce *positive symptoms*, but might allow of their development. Thus two factors are concerned in the production of a spastic paralysis: defect of pyramidal fibres causing the negative symptom, paralysis; and a resulting unbalanced over-activity of other intact centres causing the positive symptom, spasticity. It would be difficult to overestimate the value of this principle to neurology, and we must ask ourselves whether beri-beri considered from every point of view has the characters of a negative or defect disease, or whether it contains positive elements demanding some more adequate and positive explanation than mere food defect.

Before attempting to answer this question, and we think it may be answered, we must refer briefly to certain physiological observations that tend to show that Eijkman was right when he avoided the false simplicity of concluding that a 'minus' causation explained everything. Cooper and Braddon, Funk, and Caspari and Moszkowski have found that the vitamine requirements of the experimental animal vary with its carbohydrate consumption. We have seen also that when deprived of this foodstuff the fowl does not develop avian beri-beri although it takes no vitamine. There appear therefore to be two factors concerned in the production of the disease; the consumption of decorticated rice *plus* deprivation of vitamine. This aspect of the problem has been discussed by Walshe, and may be best summed up in the words of Eijkman, that even though we hold the vitamine starvation theory ('Teilhungertheorie') the ultimate cause of beri-beri may yet prove to be a nerve poison produced by a disordered metabolism arising out of vitamine deprivation.

The nervous lesion of beri-beri. Since the original investigations of Baelz, Scheube, Pekelharing, and Winkler (1882–1887) there has been a striking unanimity among pathologists that the nervous lesion of beri-beri is not specific for the disease and is not to be distinguished from that of a toxic polyneuritis. Hamilton Wright found changes in the central and peripheral nervous system like those of an alcoholic polyneuritis. L'hermitte examined the nervous system of an experimental bird dead of avian avitaminic polyneuritis and confirmed this view. He states that 'la constatation des lésions corticales est un trait de plus qui permet de rapprocher la polynévrite alimentaire avitaminique, le béri-béri expérimental, des polynévrites toxiques.' The importance of this evidence coming from an observer skilled in assessing the nature and significance of pathological changes in the nervous system cannot be overestimated.

The recent minute and extensive researches of Kimura by the most modern histological methods add to the weight of evidence and seem finally to settle this question.

Undue stress seems to be laid on two features of the morbid histology of the nervous system in beri-beri and avian polyneuritis by some observers who have approached the question from the speculative rather than from the practical point of view. These are the facts that the peripheral nerve lesion is a degeneration, and that widespread chromatolytic changes may be found in the cells of the brain and cord. In both these respects beri-beri differs not at all from the toxic polyneuritides. Polyneuritis is recognized to be a general affection of the nervous system in which certain parts prove most vulnerable. Moreover, there are no grounds for stating as both Vedder and McCarrison do that the essential lesion is not a polyneuritis, but a degenerative change in the cells of the central nervous system. Equally baseless is their conclusion that the symptoms are caused by these central lesions, for the clinical significance of these in all forms of polyneuritis is very doubtful, and there is no reason to regard them as the basis of paralytic phenomena (Oppenheim).

Further, in acute rapidly fatal beri-beri no lesions may be found *post mortem* on microscopical examination of the nervous system (Hamilton Wright), while in acute infantile beri-beri the findings in the nervous system may also be negative, or minimal.

The evidence as to the constancy of changes in the vagus nerve is most conflicting. Some observers describe them as constant, others as minimal in degree and inconstant. The point is of some importance because the characteristic acute fatal heart failure of beri-beri has been widely ascribed to this lesion, though there are no valid grounds for attributing this to vagus paralysis, which is neither a proved nor a sufficient cause of heart failure (T. Lewis). As far as is known, the cardiac lesion of beri-beri is identical with that found in diphtheria, in which a similar liability to sudden heart failure exists. Further research is needed on this point before we can say whether this is predominantly nervous or muscular in origin.

This review would not be complete without a reference to the **symptomatology** of beri-beri. This contains three elements: the nervous, the cardiac, and the oedema. The nervous symptoms considered alone do not differ in any respect from those of other forms of toxic polyneuritis. The cardiac symptoms, as has been pointed out by Stanley in a paper which the investigator of beri-beri should study closely, are identical with those of diphtheria. Beri-beri shares with this disease a peculiar and striking liability to sudden heart failure, and the fact that the heart lesion in diphtheria is responsible for this and is a fine fatty degeneration of remarkably early onset is a sound reason for regarding the cardiac symptoms of beri-beri as probably identical in origin. There is no certain lesion that can be connected with the oedema of beri-beri. Kimura points out that both nerves and muscles of the vessels show pathological changes.

McCarrison has suggested that hypertrophy of the suprarenals and excessive output of adrenalin is the cause of this symptom. But our knowledge of these structures affords no support to this view, nor is there any evidence that in cases of beri-beri which run their course to death without oedema the suprarenals differ in any way from those in the body of a case of 'wet' beri-beri.

The nature of beri-beri. The clinico-pathological study of beri-beri leads us to some very significant conclusions. We find the nervous and the cardiac lesions are identical with those produced by the action of certain well-known poisons. These lesions and the resulting symptoms are not known to be caused by any other agency than such poisons. If we are to attribute any significance at all to the phenomena of the disease in estimating its probable cause we seem forced to conclude with Eijkman, Caspari and Moszkowski and others that we are dealing with no negative or defect disease, but with a definite positive reaction of the nervous system (and the heart muscle) to some unknown poison. We know nothing of what happens in the body from the eating of a vitamine-free diet to the moment when the symptoms of beri-beri appear, and we cannot exclude the possibility that such a poison has been produced in the body. We have no analogy for such a hypothetical process as Vedder has described, nor do we find pathological evidence of it. In fact, we may even find a normal nervous system in certain acute cases. Moreover, in infantile beri-beri, examination of the nervous system reveals no imperfection of growth, or development after death. Nor during the life of the infant preceding the appearance of the disease is there any sign of defective function. Vedder's explanation that an 'essential building-stone' has been lacking in the child's nervous system from the time of its inception in the womb must therefore be regarded as merely fantastic.

There is thus seen to be a hiatus in our knowledge of the pathogenesis of beri-beri, which can only be bridged when the metabolism in this disease has been investigated and understood.

It seems probable that the study of beri-beri is peculiarly difficult in that it demands the special knowledge of investigators in widely different branches of science. A study of the clinical records shows clearly that both experimental and clinical observers have had great difficulty in assessing the nature and the significance of physical signs of nervous disorder, and no small amount of confusion has arisen from this cause.

While the cardiac pathology has never been investigated by modern methods, the biochemical investigator labours under a still greater disadvantage in that he is unfamiliar not only with human beri-beri, but with clinical and pathological observation in general. Thus he cannot readily appreciate the fundamental clinical and pathological considerations that led Eijkman, rightly, to formulate his 'roundabout explanation'.

Probably no one school of workers can justly be expected to solve all the problems presented by the deficiency diseases, and the path of progress in this field is strewn with the abandoned theories of specialists who have vainly attempted to do so. Here, more perhaps than in most practical biological problems, co-ordination between the attacking parties is needed.

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F. M. R. W.

EXTRACTION OF FOREIGN BODIES LODGED IN THE SUBSTANCE OF THE LIVER

A series of cases has been recently described to the Société de Chirurgie.

Faix of Tours communicated two observations on fragments of shell lodged deep in the liver around which an abscess had formed.

(1) A private was wounded on September 14, 1916, sustaining an injury to the knee which was treated by primary excision; also he presented a wound of entry over the right 9th rib cartilage, but no wound of exit. An X-ray photograph showed a large fragment of shell behind the 5th intercostal space in the right nipple line, which did not move with respiration but underwent slight lateral displacement when the man turned on his side. In the middle of November, two months after the injury, there was a free discharge of pus from the wound, with fever and increasing weakness. This was followed by the development of a right-sided empyema. The empyema was laid open after excising portions of two ribs, and the finger could then be passed through a hole in the diaphragm into a cavity in the liver substance. Drainage by two tubes afforded no important improve-

ment; the end of the tube passed into the excavation in the liver was found to be 4–5 cm. from the foreign body.

On January 26, 1917, i.e. 4½ months after the injury, Faix made a wide opening into the lowest part of the pleural cavity behind, by removing portions of the 10th and 11th ribs; after clearing out a large quantity of pus, the hole in the diaphragm was enlarged by cutting and the finger introduced. Under the guidance of the X-ray screen the finger was pushed on through friable liver substance until the foreign body was reached and withdrawn by forceps. It was the size of a die and surrounded by bits of flannel. The haemorrhage was arrested by plugging, and with drainage the liver tended to heal. There persisted two pleural fistulae which closed after plastic operations done in May 1917 and February 1918. Some months after the definite healing the man died of pulmonary tuberculosis.

(2) A private was wounded on October 24, 1916, by a fragment of shell, which penetrated the lower part of his chest in front, three fingers' breadth above the costal margin, and one finger's breadth outside the right nipple line. There was no wound of exit. The man picked himself up and walked 5 or 6 km. back to the ambulance, where a foreign body was found in the liver 5 to 6 cm. deep. On further examination in Paris, it was confirmed that the fragment lay in the substance of the liver 6 cm. from the surface of the anterior abdominal wall.

Three weeks after the injury an incision was made 10 cm. in length, starting from the costal margin through the abdominal wall, which exposed adhesions. On separating these pus welled up from a hole in the liver. The finger was then passed in and, under the guidance of the screen, the foreign body was found encysted, and removed with forceps. The track was plugged, tubes inserted beside the plug, and the rest of the incision sewn up. After the removal of the plug and tubes, healing progressed and the man left the hospital five weeks later quite healed.

The reporter, Lenormant, and those who discussed the communication, were agreed in the view that foreign bodies deep in the substance of the liver should not be sought for unless complicated by suppuration.

At the following meeting of the Société, however, Robineau reported cases in which he had operated in the absence of any fistula or signs of abscess formation; in one case only did he meet unexpectedly with an abscess. Haemorrhage proved controllable, but one operation had to be abandoned. Of 13 cases in which foreign bodies had lodged in or near the liver, 5 were 2–5 cm. from the surface without any external sign; 3 at least 2 cm. deep were indicated by induration on the surface; 4 formed a projection on the surface; 1 foreign body was found in the gall-bladder. 5 were on the posterior aspect and 7 on the convex antero-superior aspect. The removal was undertaken in all the cases under the guidance of the X-ray screen.

Case 1.—Wounded April 13 by a fragment of shell 8 × 10 mm. and operated on at his own request on September 20, 1916. An incision was made behind, through the 10th interspace, 8 cm. from the middle line the 10th rib was resected, and the diaphragm cut through. The liver was cut into at the point indicated but search by forceps failed. There was abundant haemorrhage and the operation was abandoned. The man was discharged 25 days later.

Case 2.—Wounded on September 22, and operated upon November 23, 1916, on account of persistent pain. A fragment of shell 10 × 12 mm. was localized under the 10th rib behind, at 7 cm. from the middle line, and at a depth of 7 cm. The 10th rib was excised, then the diaphragm and the coronary ligament cut through. An induration was felt without any surface mark over the point indicated on the screen, and at 1 cm. from the surface the foreign body was found and removed. There was little haemorrhage and he was discharged 20 days later.

Case 3.—Wounded on April 10 and operated upon on October 24, 1916, on account of persistent pain. A fragment of shell 8 × 10 mm. was localized under the 8th rib behind, at 6 cm. from the middle line and at a depth of 9 cm. The 8th rib was excised, then the pleura and diaphragm incised, when at the point indicated by the screen the foreign body was felt and removed. There was little haemorrhage and the man was discharged on the 15th day.

Case 4.—Wounded on August 20, 1914, and operated upon at his own request on April 18, 1916. A rifle bullet, the nose pointing downward, lay under the 11th rib behind near the spine; the base of the bullet was 7·5 cm. deep. The 11th rib was excised, the pleura and diaphragm cut through, and the peritoneal cavity opened above the right kidney. The point of the bullet was felt projecting, the base was buried in the coronary ligament. There was considerable haemorrhage. The man was discharged on the 25th day.

Case 5.—Wounded on September 10 and operated upon October 24, 1916, on account of pain. A fragment of shell 12 × 24 mm. underlay the 9th rib on the left side, 6 cm. from the middle line and 9 cm. deep. The 9th rib was resected and dense adhesions between the lung and diaphragm separated, the diaphragm was cut through, and under the guidance of the screen the foreign body was found buried in thick adhesions between the diaphragm and liver, from which it was removed with slight haemorrhage. After dyspnoea for two days the man recovered and was discharged on the 24th day.

Case 6.—Wounded on October 10 and operated upon on November 18, 1915, on account of pain. A fragment of shell, the size of a lentil, underlay the 9th rib of the right side, mid-way between the back and front. After excision of the 9th rib, and cutting through the pleura and diaphragm, a dense adhesion to the liver was met with, and at a depth of 2 cm. the foreign body was found and removed. There was little haemorrhage, and the man was discharged on the 21st day.

Case 7.—Wounded on August 24 and operated upon on December 8, 1917, on account of pain and dyspnoea. A fragment of shell 8 × 12 mm. lay behind the 4th rib in front in the right nipple line, at a depth of 5 cm. The 4th rib was resected, adhesions between the lung and diaphragm separated, the diaphragm incised, an induration felt on the surface, and the foreign body reached 1 cm. beneath the surface. Free haemorrhage was controlled by plugging. Discharged on the 30th day.

Case 8.—Wounded, and later operated upon on December 12, 1918, on account of pain localized at the situation of the foreign body. A fragment of shell, the size of a haricot bean, was placed behind the 9th rib, in front, at a depth of 3–4 cm., and under the 8th rib behind at a depth of 7 cm. The 9th rib was removed over the point indicated, and the pleura and diaphragm incised, when slight adhesions were met with. There was no induration on the surface, but a grooved needle struck the foreign body at 4 cm. from the surface. Removal set up free haemorrhage which was checked by digital pressure, and the man was discharged on the 21st day.

Case 9.—Wounded on March 5 and operated upon on October 25, 1916, on account of intense and fixed pain. Two fragments of shell in contact, 15 × 30 mm. were found behind the base of the xiphoid cartilage, just to the right of the middle line, at a depth of 4·8 cm. The right chondracostal border was excised and the peritoneum peeled off the diaphragm until a firm adhesion was reached which was cut into, when pus mixed with bile escaped. The foreign bodies were found loose in the cavity which had excavated the convex surface of the liver under the diaphragm. The cavity was wiped out and drained. The pus contained *Staphylococcus albus* and pneumo-bacilli. There was an irritating discharge of bile and pus, but the sinus had closed by the 82nd day.

Case 10.—Wounded on April 19 and operated upon June 9, 1917, for pain localized at the situation of the foreign body. A small fragment of shell 6 × 6 mm. lay under the right costal margin in the nipple line at a depth of 7·5 cm. The costal margin was cut away, there was no mark on the surface of the liver; exploration at the point indicated on the screen just above and external to the gall-bladder, led to the foreign body at 5 cm. from the convex surface. There was free haemorrhage, incompletely arrested; suppuration followed, pus and bile being discharged. Healing occurred in 36 days.

Case 11.—A fragment of shell, the size of an almond, was buried in the right lobe of the liver at a depth of 4 cm. It was reached with difficulty by pushing in forceps under the guidance of the screen. The haemorrhage was checked by finger pressure and healing followed.

Case 12.—Operated on account of pain. A fragment 12 × 15 mm. was placed behind the anterior costal border in the right nipple line. It was found under the liver, where it projected from the surface. Moderate haemorrhage was set up which was checked by pressure, and the patient was discharged on the 20th day.

Case 13.—Wounded on October 9, 1915, and operated upon on February 16, 1916, on account of attacks of pain. A fragment of shell, the size of a lentil, was placed behind the right costal margin 8 cm. from the middle line at a depth of 5 cm. A distended gall-bladder was met with and a search made on either side of it. Then the gall-bladder having been partly freed from the liver, it was noted that the foreign body moved with the gall-bladder. The foreign body was indeed impacted in the neck of the gall-bladder, but it could not be felt from the outside. The gall-bladder was excised and the man discharged on the 20th day.

Robineau was very successful under the guidance of the X-ray screen in removing the foreign bodies without setting up more haemorrhage than could be controlled by pressure. In only one case had the operation to be abandoned. The main objection may be said to lie in the small size of the foreign bodies; only in one case was there suppuration, but several of the men continued to feel pain. There is this to be said, that even the smallest and most quiescent fragments had septic organisms on their surface. Hence, in the end, suppuration might have supervened had the foreign bodies not been removed.

Soubeyran of Montpellier had collected 297 observations on wounds of the liver and biliary passages since the commencement of the war—which presented great differences in course. In some cases death soon occurred from suppuration; in other cases foreign bodies had remained in the liver for more than two years without causing disturbance. He had himself observed 27 cases of wounds of the liver; in 7 no foreign body had lodged; in

9 the wounds were explored on account of haemorrhage and the foreign body removed at once, 5 recovered and 4 died. In one case fatal tetanus prevented operative interference. In 10 cases expectant treatment was adopted; 4 recovered without removal of the foreign body; in two the foreign body was removed; 4 died.

Faix. Deux cas d'extraction secondaire de projectiles du foie suivis de guérison. [**Two cases of secondary extraction of projectiles from the liver followed by healing.**] *Bull. et mém. Soc. de chir. de Par.*, 1919, **45**, 1407.

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W. G. S.

DECAPSULATION AND NEPHROTOMY FOR NEPHRITIS

The idea of tension arising in the kidney enclosed within its capsule, and the mechanical relief of that tension occurred to Reginald Harrison in 1896. The recognition of such a state of tension was a novelty; it may be quoted as another instance of the advantage to be gained by a study of the 'Pathology of the Living', over that of the 'Pathology of the Dead'. In the living a kidney might feel stony hard, have a colour bluish or blackish red, and its substance bulge out through an opening in the capsule, whereas the same kidney on the post-mortem table would then feel flabby, look pale, and its cut section have lost the appearance of vascularity.

Among clinical signs of danger, attention had been mainly directed to those of uraemia, acute or chronic. The term anuria, so late as 1883, in Quain's *Dictionary of Medicine*, was defined as absence of urination, without differentiation between suppression and retention of urine. In the article 'Disorders of Micturition' Henry Thompson did not mention anuria. Also the article by Grainger Stewart on 'Obstructive Suppression of Urine' did not refer to the application of the term 'Anuria' made by William Roberts of Manchester. In his *Practical Treatise on Urinary and Renal Diseases*, 3rd ed. 1876, Roberts distinguished under 'Anuria' the cases of patients suffering from blockage of both ureters by calculi in which, except for the absence of urine passing into the bladder, there was a lack of signs, not only of those pointing to uraemia but also of signs attached to renal colic. Only after days or a week, did uraemic signs such as muscular twitchings set in, and only slight indications of uraemia preceded death. Special attention was devoted to what was distinguished as 'Obstructive Suppression' by Fagge in 1886, who at the same time characterized uraemic symptoms as connected with 'non-obstructive suppression'. The clinical features of anuria as defined by Roberts thus served as a call to the surgeon to perform bilateral nephrotomy. It has turned out, however, that 'anuria' in the sense used by Roberts occurs with 'non-obstructive suppression' at any rate for days before the symptoms of uraemia set in shortly before death.

In 1896 Reginald Harrison drew an analogy between tension within the capsule of the kidney which checked the circulation through the organ and prevented the excretion of urine, and that of glaucoma which was treated by iridectomy. Also for the relief of pain in acute epididymitis, the fibrous capsule of the epididymis had been incised. At that time diagnosis was not aided either by X-ray photography or by the cystoscope, and in three cases Harrison had operated for suspected suppuration in the kidney caused by calculus. One case proved to be nephritis following scarlet fever in a girl ; in a second, nephritis had been set up by cold and damp ; in the third, nephritis had followed an attack of 'influenza'. All three cases were relieved by nephrotomy and temporary drainage from the pain, swelling of the kidney, and the albuminuria from which they had suffered previously to the nephrotomy. In support of his argument in favour of tension within the renal capsule, Harrison quoted statistics of 5,109 cases of scarlet fever, 55 of whom had died of nephritis. At the post-mortem examination of a girl aged 7, who had died four days after complete suppression of urine, both kidneys had been found intensely congested.

Harrison returned to the subject in 1901, but did not make any further additions ; the fresh cases he mentioned were those of suppuration following stone or injury.

In 1899, Edebohls (1) of New York published a paper entitled 'Chronic Nephritis affecting a Movable Kidney as an indication for Nephropexy', and in 1901 he made another communication on 'The Cure of Chronic Bright's Disease by Operation, i. e., by Decapsulation'.

The free use of the term 'Bright's Disease' has hindered matters because it has been used for two different conditions, the one localized in the kidneys, and the other in which the cirrhotic or granular kidneys form but a part of a generalized affection. It is obvious that in the latter case no mechanical relief of tension by division of the capsule of the kidney can be of service, and to operate in such cases has only tended to throw discredit upon the whole proposal. Edebohls in 1899 reported that in four out of six women suffering from movable kidney, the urine contained both albumin and casts. Improvement followed decapsulation and nephropexy ; in one case the operation was done on both sides in 1898, and the urine was free from albumin and casts in 1901.

Edebohl's proposal in 1901 (2) was to treat in this way all cases of chronic Bright's disease. Of 191 cases submitted to nephropexy, 16 were found to be suffering from chronic nephritis, and he reported that in January 1898 he had decapsulated the kidneys in a case of chronic Bright's disease although the kidneys were not movable.

In 1903 (3) he claimed to have done 51 cases of renal decapsulation for chronic Bright's disease. 47 on both sides, 7 cases had died within 17 days of the operation and 7 within 2 years, 2 had not improved, and 22 were improving.

Edebohl's assumed that by decapsulation there was set up an anastomosis between the renal arteries of the cortex and the perirenal tissues. This was proved to be wrong: both after experimental decapsulation in dogs, and on post-mortem examination of kidneys which had been decapsulated for nephritis, there was found a thick layer of scar tissue enclosing the kidney so as to form an inflammatory capsule thicker than the normal one, and no vascular connexions between the cortex and the surrounding tissue through the capsule could be made out.

Edebohls, before his death in 1912, had operated on 102 cases. In 3 the result was unknown.

10 died within 2 weeks.

39 died later; 29 from chronic nephritis, on an average 17 months after the decapsulation, 10 from causes said to be unrelated to chronic nephritis,

50 were then living. 6 unimproved. 11 improved. 33 free from albuminuria and casts between 15 months and 14 years 10 months from the decapsulation.

In the cases of interstitial nephritis, the urine became free from albumin after decapsulation on an average in 6 months, in the cases of parenchymatous nephritis on an average in 14 months.

In 1916 Lloyd in New York reported 25 cases, 15 classed as parenchymatous and 7 as interstitial nephritis. After decapsulation, 2 of the parenchymatous cases died, the rest improved, one in particular almost blind beforehand from albuminuric retinitis. All the 7 interstitial nephritis cases died without improvement. In 146 operations the mortality had averaged 10 per cent.

Tyson in 1911 reported the following four cases:—

Case I.—A girl aged 9 had suffered from scarlet fever at the age of 4 followed by acute nephritis. Upon this supervened chronic nephritis with five acute recrudescences. After the last of these there was general anasarca and ascites; the eyes were almost closed and the abdomen enormously distended. The urine averaged 20 oz. in amount, sp. gr. 1016, albumin a half—pale granular casts. After a course of medical treatment combined with paracentesis for two months she was no better. A repetition of the paracentesis combined with decapsulation of the right kidney was followed by an immediate improvement. The urine rose in quantity to 60 oz.; the anasarca and ascites disappeared and the albumin fell to one-tenth whilst in bed, but on getting up it increased again to one-half. Two months later decapsulation was repeated on the left kidney, six months later she had the look of health, the albumin was one-third with a few hyalin casts. One year after the second decapsulation she was attending school during a severe winter, when she relapsed and died.

Case II.—A boy aged 15 had had scarlet fever three years before. Dropsy had been noticed for three months; there was then extreme general anasarca, the eyes were almost closed, the penis and scrotum were involved. There was some free fluid both in the peritoneal and pleural cavities but there were no retinal haemorrhages, nor signs of uraemia. The urine became almost solid on boiling and there were casts, both granular and hyalin; the quantity averaged 6–8 oz., the sp. gr. 1016. After three months of medical treatment, as there was no improvement, both kidneys were decapsulated at one sitting. Two months later the boy was free from signs of dropsy. The urine contained much albumin but less than before the decapsulation; nine months later he was working as an apprentice to a carpenter, and working every day. The albuminuria had persisted and there were hyalin and granular casts.

Case III.—A girl aged 17 had had a year before an attack of tonsillitis and swelling of the glands in the neck. The urine then contained $\frac{1}{8}$ of albumin. The tonsillitis recurred and was complicated by pneumonia.

After this the feet swelled, she became weak and had headaches. The urine was scanty, albumin $\frac{2}{3}$ with casts. She was not improved by three months of medical treatment during which the quantity of urine varied between 43 and 18 oz. Decapsulation was done on both kidneys, from which she made a good recovery. The albumin became reduced to $\frac{1}{8}$. Seven years later she was working in a store and kept well on the whole. She occasionally needed medical treatment for recurrence of symptoms. The urine still contained much albumin and hyalin casts.

Case IV.—A male aged 32 suffered from nephritis after getting wet. Nine months later he was suffering from intense headache, nausea and vomiting; the quantity of urine had diminished in spite of active medical treatment, sp. gr. 1008–1012—acid—$\frac{1}{3}$ albumin, numerous hyalin and granular casts. On decapsulation the kidneys proved typically 'granular', a good deal of blood was lost at the operation, which was done with the man in a desperate condition, and he died five hours later.

In 1916 Burns described the case of a girl aged 6 who after an illness of three weeks, ? scarlet fever, had swelling of the body and eyes. Under a course of medical treatment the quantity of urine fluctuated between 10–40 oz. with 1–16 grs. of albumin per oz. As no improvement followed, both kidneys were decapsulated by Alexander Miles. The kidneys were large and congested, with one or two pale areas. At first there was slight improvement which after a fortnight became more rapid, the dropsy disappeared, the quantity of urine averaged 25 oz., the albumin $\frac{1}{2}$ gr. to 1 oz. The child became lively and looked in good health. There was a trace of albumin on her discharge.

Chiari's case was that of a soldier aged 33 who, after suffering for months from severe chronic nephritis accompanied by general oedema, high blood-pressure, persistent headache, retinal haemorrhages, albumin 10–12 pro mille Esbach, granular casts with many red blood corpuscles—was attacked by uraemia. The right kidney was then decapsulated; it was abnormally large, hard and dark red. There was immediate improvement; the next day the quantity of urine was 3,000 c.cm., and the day following 5,000 c.cm. The oedema disappeared, the albumin came down to 0·5–1 per cent.; there was no more haematuria: the retinal haemorrhages disappeared. The indigo-carmin colour appeared in 8–10 minutes in the urine after subcutaneous injections.

Morse in 1917 reported the following four cases of chronic nephritis in children.

Case I.—A boy at the age of 3 had acute nephritis. At 6 there was a subacute exacerbation surpervening upon chronic nephritis, attended by ascites and general oedema. Both kidneys were decapsulated, neither were enlarged nor pale. At first he appeared worse, then there was gradual improvement; two years later he was well and the urine had been free from albumin for 8 months.

Case II.—A girl aged $5\frac{1}{2}$ had had tonsillitis two months before, which was followed by acute nephritis. She was in bed for 8 months when the right kidney was decapsuled, the left kidney was represented merely by a small soft mass. There was a rapid recovery of apparent health. A year later the urine was of low specific gravity and there was a trace of albumin but the girl looked well.

Case III.—A girl aged 10 had had chronic nephritis for a year. Decapsulation was done and $1\frac{1}{2}$ years later she had much improved.

Case IV.—A boy aged 9 with marked subacute parenchymatous nephritis was decapsuled. Some improvement followed, but he had to be tapped again. Then he recovered so far as to be able to go to school. His urine was of low specific gravity and contained much albumin.

Morse collected 19 cases in which decapsulation had been done in children.

4 died on the 5th, 6th, 15th, and 18th day after the operation.
3 cured, i.e., presented no abnormality 4 months, 6 months and 9 years after.
7 apparently well, but the urine contained albumin and casts.
1 recurred after having had normal urine for 2 years, the decapsulation was repeated a second time and death followed 6 weeks later.
2 not improved, living 5 weeks and 6 months after.
2 improved for a time. 1 recurred and died a year after. 1 had broncho-pneumonia and died 4 months after.

Cassel in Berlin noted the case of a girl aged 9½ who a month before had been attacked by general dropsy and albuminuria, it was not known why. At the end of a month a severe attack of uraemia set in which was at first partially relieved by medical treatment including venesection and leeches to the mastoid region. Paracentesis abdominis yielded 2,000 c.cm. of pure serous fluid. Six weeks later a second attack of uraemia occurred which now resisted medical measures, so after four days both kidneys were decapsuled. The soft parts around were oedematous, the kidneys much enlarged, brownish red, smooth under the capsule which was very tense and easily stripped off. The next day 220 c.cm., and on the second day after the operation 910 c.cm. of urine were passed. Convalescence was checked by an attack of faucial diphtheria which yielded to serum. A month after the decapsulation a second paracentesis abdominis was performed, 2,400 c.cm. of fluid were collected and much more escaped later. A third paracentesis was required three months after the second, when 2,200 c.cm. of serous fluid were drawn off. The urine then had 12 pro mille of albumin with a few casts. Eleven months after the bilateral decapsulation all signs of dropsy had gone—the child was fat, weighing 36 kg. Pulse 100–120, urine 700 c.cm., albumin 1 pro mille, no casts, a few epithelial cells. Six years later there was a trace of albumin; otherwise she appeared well.

Eclampsia before and after delivery. In 1903 Edebohls decapsulated the kidneys in a woman who had been delivered and the eclampsia was arrested.

In 1904 (4) he reported a second case in which a woman near term was attacked by eclampsia and almost complete suppression of urine. Decapsulation arrested the convulsion and the flow of urine was re-established. Two days later she was delivered of twins. One died soon after birth; four and a half months later both mother and the remaining child were in perfect health. Thus decapsulation had proved a superior measure to forced delivery.

In 1909 Halliday Croom performed decapsulation to relieve a primipara aged 26 who had been beforehand in good health and had been delivered of a healthy child. Eclampsia set in which was not relieved by medical treatment. Both kidneys were decapsulated, the right kidney appeared enlarged, the left normal. Within the next 24 hours 90 oz. of urine were passed; the albuminuria disappeared and the patient made a good recovery. He collected 26 cases and concluded that for eclampsia before delivery labour should be induced; after labour decapsulation should not be delayed until there was complete anuria.

Jullien in 1919 reviewed the cases in which decapsulation had been done for puerperal eclampsia and considered that it should be done only when anuria had set in. Then in 80 per cent. after bilateral decapsulation, the urinary secretion becomes established. But on account of other changes in the liver and brain the mortality from eclampsia extends to 40 per cent., and this cannot be prevented by decapsulation of the kidneys. Thus his second conclusion contradicts his first that anuria should be awaited before proceeding to decapsulation.

Clifford White, in six cases in which he performed Caesarean section in place of forced delivery, felt the kidneys to be stony hard. He exposed the right kidney from the peritoneal aspect and made an incision along the convex border, the incision penetrating a little into the cortical substance. A counter-opening for drainage was made through the right loin, after which the abdomen was closed.

Non-obstructive anuria—its pathology. In 1898 Rose Bradford and T. W. P. Lawrence under the title 'Endarteritis of the Renal Arteries causing Necrosis of the entire Cortex of the Kidneys', described the examination *post mortem* of a woman aged 35, who had been well until she gave birth to a dead child. This was followed by almost complete anuria until her death seven days later, during which only a few teaspoonsful of urine containing albumin and pus were passed. She had no fever nor signs of uraemia but clinically resembled a case of obstructive suppression of urine. The kidneys were not markedly enlarged; the cortex was entirely necrotic except for a narrow zone bordering on the medulla and another immediately under the capsule. The epithelium of the tubules, and to a less extent that of the glomeruli, failed to stain with logwood and there was thrombosis of all the interlobular and glomerular arteries. There had been no previous intestinal fibrosis. In the narrow zones where there was not necrosis, there was a recent small cell infiltration. Bradford and Lawrence considered that the arteries had been thickened by a previous endarteritis, presumably of long standing, and that the thrombosis setting up the necrosis had followed upon the still birth. The case appeared to resemble that produced in an animal by removal of both kidneys or by the ligature of both ureters, after which the animal dies about the third day without signs of uraemia.

Herringham and Thursfield described the early changes differently. The specimen examined was from a woman aged 20 in whom dropsy and anuria followed pregnancy. The first change appeared to be an epithelial proliferation of the cells of the capsule of the glomerulus, an exudation of serous fluid, and a collection of cells within the capsule which gradually obscured the capillary tufts. But until they were obscured both the afferent and efferent artery of the glomerular tufts appeared to be patent. The onset in this case was no doubt slow, but it would appear that the thrombosis may be regarded as secondary to an acute serous exudation and epithelial proliferation.

In support of the above Griffith and Herringham described the case of a woman aged 35 who had suffered from chronic nephritis for five years, for which she had been under treatment. She was delivered of a dead child and 12 oz. of old-standing clot were removed at the same time. From that day until her death 9½ days later, she passed only 9 oz. of urine. Nephrotomy was considered contra-indicated because the suppression was deemed due to interstitial nephritis and not to congestion. Symptoms of uraemia were absent practically until the end. After death there was found slight hypertrophy of the heart and old-standing chronic interstitial nephritis. There was necrosis of the renal cortex of both kidneys, together with thrombosis of the cortical arteries, similar to that described by Bradford and Lawrence.

Lloyd of Melbourne described a similar case. A woman aged 39, after giving birth to a still-born child, only passed 11 oz. of urine until her death 11 days later; slight symptoms of uraemia appeared towards the last. The post-mortem examination showed old-standing chronic interstitial nephritis and recent necrosis of the cortex, but there were no signs of endarteritis.

H. D. Rolleston referred to 11 cases of symmetrical cortical necrosis, generally following delivery of a still-born child. The symptoms mainly resembled those of calculous anuria and any symptoms of uraemia were only slight. In some there was evidence of previous chronic nephritis but not in all. The anuria lasted from 1½ to 11 days before death. The morbid lesions consisted in a symmetrical necrosis of the renal cortex, thrombosis of the cortical vessels, also usually thrombosis of the interlobular arteries supplying the cortex. In some there was a narrow rim of unaltered cortex underneath the capsule. Toxaemia when less severe appeared to cause degeneration of epithelial cells; if more severe there was thrombosis followed by necrosis.

An explanation of the symptoms of anuria rather than of uraemia was that in anuria there was little absorption from the kidneys to affect the rest of the system. Thus the cases resembled in their course that following the removal of both kidneys from animals or the accidental removal of a single kidney in a man or the obstruction of both ureters. In uraemia and eclampsia there was much toxic absorption from the kidneys, in anuria apparently very little.

In 1913 Jardine and Kennedy in Glasgow published three cases of symmetrical necrosis of the cortex of the kidneys occurring in women post-partum. Jardine had previously described two cases. In the three cases the anuria before death existed for 4½ days, 2½ days, and 1½–2 days respectively. In all three cases the kidneys appeared to have been previously healthy, and the changes leading up to the necrosis seem to have corresponded with the changes described by Herringham and Thursfield rather than with that of a primary infective thrombosis. Jardine viewed decapsulation as useless. Kennedy in a letter kindly informed me that another case had recently occurred in which death followed after 5 days of anuria. No changes were found in the liver. Decapsulation was done without effect.

In 1904 Meinhard Schmidt operated on a boy aged 5, who had had anuria for four days whilst peeling from an attack of scarlet fever three weeks before. The kidneys were neither palpable nor tender. They appeared somewhat enlarged, of a dark reddish-brown colour, and had the elasticity of a ripe plum. Decapsulation of both kidneys was done, and some punctures made with very little loss of blood. Three hours after he passed 200 c.cm. of pale bright green urine, in it were a few epithelial cells, leucocytes and granular casts with a cloud of albumin. Recovery occurred in a month, and there was then no albuminuria.

Gümbel operated on a more unfavourable case. A ricketty girl aged 6, a cripple, had parenchymatous nephritis following whooping-cough and measles. For four days there was complete suppression of urine and symptoms of uraemia had supervened when the right kidney was decapsulated. Secretion of urine followed containing albumin 7 per cent. Five weeks later she had much improved ; there was only a trace of albumin, and there were no epithelial cells or casts.

In 1913 Herz reported the case of a girl aged 8 who had been under treatment for months on a milk diet. Albumin about 15 pro mille. For two days there was anuria, then the left kidney was decapsuled and forthwith 400 c.cm. of urine was passed, and 500, 700, and 800 c.cm. on the following days. After temporary general improvement the quantity of urine relapsed to 100–200 c.cm. ; there was marked increase of oedema and threatened uraemia. Nineteen days after the left, the right kidney was decapsuled, and this was followed by progressive improvement. The quantity of urine rose to 1,000–1,500 c.cm., albumin 2–5 pro mille—the oedema disappeared. Ten months later she was well and at school. She had then no albuminuria.

Harris and Clayton Greene observed the case of a girl aged 18 who, after swallowing 26 gr. of solid corrosive sublimate, had 36 hours later total suppression of urine. On the third day of the anuria the right kidney was incised and drained. Directly afterwards 4½ oz. of urine were passed containing only 0·5 per cent. of urea. The fourth day 2½ oz. of urine were passed. On the fifth day the left kidney was incised and drained. Both kidneys were enlarged and congested, but the left in the meantime had become larger and there was more perirenal oedema. 12 oz., 28 oz., 30 oz., 40 oz. were passed on the following days. Then between 30 to 40 oz. until two days before death on the sixteenth day from mercurial colitis. At the postmortem examination the kidneys showed no evidence of nephritis.

Tisseraud of Lyons reported two similar cases. Mercurial poisoning set up suppression, and decapsulation restored the flow of urine, although both patients died from the effects of the mercurial poisoning.

Spencer observed the following case. An engineer aged 36, whose urine contained a trace of albumin, underwent the operation for the cure of a right inguinal hernia. On the twentieth day after the operation he was up and about the ward preparatory to being discharged when he was attacked by dull aching pain in the loins and vomiting. On the three following days he passed 12 oz., 10 oz., and 8 oz. of urine which contained not more than a cloud of albumin, a few red cells and no casts. On the fourth day he had three uraemic convulsions in succession, and when the operation was begun he was half unconscious and his breath had a urinous odour. Bilateral nephrotomy was done and a drain inserted into each kidney. The kidneys were about double the normal size and congested, but there was no important haemorrhage. Urine escaped freely from both wounds shortly after the operation. Gradually the urine passed into the bladder, and within two months both wounds had healed. The urine then averaged about 80 oz. per diem, the sp. gr. 1006, and it contained a cloud of albumin. On discharge he was given strict injunctions. He attended the hospital 7½ years later in good health. He had kept strictly to the diet ordered. During the war he had frequently to work from 16 to 20 consecutive hours. Some urine passed after his dinner contained the merest trace of albumin, the urine next morning presented a cloud.

Arthur Evans operated upon a boy aged 11 for acute appendicitis, and a drainage tube was inserted. Four days later pain in the loins and vomiting set in followed by suppression of urine. On the fifth day uraemic convulsions supervened, and when operated upon he was unconscious and the pulse just perceptible. Bilateral nephrotomy was rapidly done and a bit cut out of one kidney. Both kidneys were larger than normal and more tense. There was no urine in either pelvis, but two hours after the operation the dressings were soaked with urine. The wounds healed and the urine became normal. Hebb reported on the piece removed: 'Malpighian bodies large, and the capillaries engorged; in some there is a coagulum. The lumen of the tubules is large, the lining cells are small and finely granular, the nuclei are normal. Some tubules contain a finely granular detritus, and others a homogeneous substance (possibly casts). The condition is of recent origin. There is no evidence of septic inflammation or of any growth. The kidney is in a condition of 'cloudy swelling'. It is clear that the case was one of suppression of urine in a patient whose kidneys were previously normal. The boy attended the hospital six years later for inspection; he was in perfect health, with normal urine and said that he never felt anything of the renal scars.

A case in which nephrotomy on one side only was apparently insufficient. Holmes of Warrnambool, Australia, had under his care a boy aged 20 months. When 11 months old he had an attack of pneumonia from which he seemed to completely recover, but subacute parenchymatous nephritis as a sequela was not excluded. He was suddenly attacked; suppression of urine followed, and definite uraemic symptoms appeared after a week. The right kidney was cut into through oedematous tissue, it appeared quite black; the pelvis was incised and a drain inserted. The dressing was quickly soaked with urine, the uraemic symptoms subsided and he became conscious, but no urine passed into the bladder. The child relapsed three days after the single nephrotomy and he died on the eleventh day of illness. As there was no *post mortem* the state of the left kidney remained undetermined; but the right kidney was not noted to be large, as if a single kidney.

A case in which decapsulation without nephrotomy appears to have proved insufficient. A woman aged 32, under Bode of Homburg, had passed no urine, except driblets, for 10–15 hours, and complained of headache, malaise, flatus, and constipation. The illness had begun half a year before with severe pain in the left loin radiating towards the bladder. Medical treatment was tried, but the anuria persisted and uraemic symptoms began to appear. Decapsulation was done on the left kidney; there was much perirenal oedema, the kidney was four times the normal size, of a bluish-red colour, and the substance bulged through the incision made in the capsule. After decapsulation the kidney became visibly smaller and redder. An hour later 400 c.cm. of turbid acid urine was passed, sp. gr. 1006, with albumin and red blood corpuscles but no casts. In the next 24 hours 2,350 c.cm. of urine was passed. Improvement followed and the woman began to get about after the wound had healed, but a fortnight later she was again the subject of anuria and increasing threats of uraemia. The wound was consequently reopened, and a thick adhering false capsule separated. She was again relieved, and 2,250 c.cm. of urine passed on the following day. It was then found by means of the cystoscope that no urine escaped from the right ureteral orifice. Three weeks after leaving the hospital for the second time she was readmitted in a third but milder attack which yielded to medical treatment. Six weeks after the third attack she was readmitted in a more severe one; the false capsule was again separated; this third operation was followed by severe collapse, no flow of urine followed, uraemia and death supervened. At the *post mortem* a left single kidney was found; it was partly necrosed as the result of large and small thrombi, haemorrhages, small abscesses and pus in the tubules, but an absence of old-standing interstitial nephritis. The right kidney and ureter were absent, a slight depression of the mucous membrane on the inner surface of the bladder occupied the position of the orifice of the right ureter.

Septic infections of the kidneys. At the International Medical Congress held in London in 1913, Brewer opened the discussion by distinguishing infection (1) through a direct penetrating wound; (2) extension from a neighbouring focus; (3) ascending from the lower urinary passages; and (4) of haemic origin, the infection arriving by the blood-stream. Confining attention to the last category, it had been noted after pyaemia and septicaemia including relatively insignificant peripheral infections such as infection of a finger; it had followed erysipelas, endocarditis, quinsy, and Lannelongue observed seven cases following infective osteomyelitis. Staphylococci and streptococci are the infecting micro-organisms. Experimentally in animals embolic infection is invariably parenchymatous; pyelitis is never so produced. The suppuration complicating *coli* bacilluria is quite different: it starts as a pyelitis.

The haemic parenchymatous infections may be divided into

(1) Acute fulminating; liable to be fatal, even although there is merely the kidney lesion. If limited to one kidney the essential treatment is nephrectomy.

(2) Subacute; it is difficult to recognize until one kidney has been destroyed.

(3) Mild and insidious; e.g. during convalescence from typhoid fever.

Diagnosis. (1) The acute form may be expected to begin with a rigor and a temperature of 104–105° F., the pulse-rate being 120 or more. At first the pain may be widespread, but it tends to become concentrated with acute tenderness at one costo-vertebral angle, especially on the right side. The urine is apt to vary, sometimes it may be found normal when coming only from the opposite kidney, otherwise mixed with blood and pus.

(2) The subacute form may be at first confused with appendicitis, cholecystitis, [or even with abscess of the liver; a renal abscess develops, pyonephrosis and perinephritic abscess follow.

(3) It is especially difficult to differentiate it when on the right side from subacute appendicitis. When on the left, the costo-vertebral tenderness will be marked.

Treatment. (1) For the fulminating type affecting only one kidney immediate nephrectomy is indicated, for there are multiple abscesses throughout the renal cortex. Of 16 cases, 2 died untreated within 12 days of the onset; 4 submitted to nephrotomy and drainage, all died; 10 upon whom early nephrectomy was done, all recovered.

(2) Early decapsulation with opening of an abscess, or nephrotomy and drainage is called for; if there is delay nephrectomy may become necessary. 18 cases had been operated upon with no deaths, one case required a secondary nephrectomy.

(3) The mild and insidious type requires observation under treatment by rest, abundance of water, and administration of urotropin.

Two cases in which nephrectomy was done in consequence of infection from a finger. In Fischer's case a woman aged 24 acquired septic infection of a finger which was incised. Three weeks later she was attacked by acute pain in the right renal region, there was high fever and leucocytosis. A perinephritic abscess was diagnosed, which was opened, but the kidney was not explored. As no improvement followed this was done three weeks later, when the upper part of the kidney was found to have been destroyed by an abscess containing *Staphylococcus pyogenes aureus.* Recovery followed upon nephrectomy.

In McWilliam's case a woman aged 38 had a whitlow ending in necrosis of the index finger. Three weeks later there occurred the first sign in the right renal region which was diagnosed as a perinephritic abscess and laid open. A fortnight later the kidney was explored, three abscesses were found containing *Staphylococcus aureus.* Nephrectomy and amputation of the finger were followed by recovery.

It may be suggested that if in the two cases the kidney had been cut into at the first operation, nephrectomy would have been unnecessary. In support of that the following may be cited :

In January 1919, a sister of a surgical ward at the 4th London General Hospital, R.A.M.C., T.F., a spare woman, who had worked hard throughout the war among septic cases, presented no definite sign of septic infection. She was suddenly seized with acute pain in the right renal region and frequent micturition. Her temperature was 103·8° F., pulse 108, and respirations 34. Herpes appeared on the lips and the tongue was coated and dry. There was acute tenderness and rigidity over the right kidney. The urine which was frequently passed was at one time clear and normal, and at another it resembled in colour and consistency a cupful of chocolate. Only *Bacillus coli* was found in the urine, and there was no sign of calculus shown by the X-rays. Nephrotomy was done on the third day, the perinephritic tissues were oedematous and blood-stained, the kidney was swollen and tense. On incising the capsule more blood-stained oedematous fluid escaped. The kidney cortex was a dusky red. The finger was pushed through to the pelvis which was not distended, and along the track a tube was inserted. There was immediate relief. The following day the temperature was 99° F., the pulse-rate 88, and the respirations 18, the urine by the bladder was blood-stained, but no longer like chocolate ; the flow of urine from the wound was blood-stained, but there was no marked haemorrhage. The drainage tube was removed after five days, and she was able to leave the hospital, with the wound healed, in a month. The urine still contained some *Bacillus coli.*

Conclusions. (*a*) All the various cases cited above confirm the necessity of recognizing the existence of tension within the capsule of the kidney to which attention was drawn by Reginald Harrison.

(*b*) Edebohls introduced the operation of decapsulation and it has proved of great importance in suitable cases. He was wrong, however, in attributing the effect to an anastomosis between the renal and perirenal vessels. The reverse happens and is confirmed by animal experiments ; the new false capsule is more dense and adherent than the normal one, and there is less of anastomosis between the superficial vessels of the renal cortex and the new false capsule than there is between the cortical vessels and the normal capsule. Edebohls was also wrong in styling decapsulation a cure for chronic Bright's disease.

(*c*) The operation is useless and is contra-indicated for adults suffering from chronic interstitial nephritis, the so-called granular kidney, along with the generalized conditions attending that state of the kidneys. Many more instances of the failure of operative treatment might have been quoted.

(*d*) Decapsulation has succeeded in cases of subacute parenchymatous nephritis of children, even when complicated by general anasarca, ascites, &c. But no cases have been cured; the use of the word 'cure' is harmful. The best of the cases have remained for years in apparently good health, but with some albuminuria. The decapsulation should be done as soon as it is clear that improvement does not follow quickly upon medical treatment. It should be done on both sides, preferably at the same operation; there is no fear of shock or haemorrhage. When the second decapsulation has been put off, more oedema, swelling and congestion of the second kidney, as compared with the state of the first is met with.

(*e*) Decapsulation is a means of reducing the mortality from eclampsia, said to be some 40 per cent. in the case of the mothers, not to speak of the foetus. Bilateral decapsulation on the first onset of eclampsia, especially when there is evidence of pre-existing chronic nephritis, offers the best chance for both mother and child. Eclampsia when well established appears to be best countered by Caesarean section: it avoids the injuries connected with forced delivery and affords a chance of saving the child. It also gives an opportunity for feeling the kidneys through the abdominal cavity. When felt enlarged and stony hard one kidney at least should be decapsuled and a counter-opening made in the loin.

(*f*) There are good reasons for distinguishing from eclampsia the cases of post-partum bilateral cortical necrosis. Clinically the cases begin as anuria and any uraemic symptoms are late. Moreover the lesions occurring in eclampsia in the liver, brain, &c., have been absent or occur only shortly before death. The view should be taken that the still-birth, &c., occasions an acute toxic exudation within the capsule which may be relieved before there is widespread thrombosis in the cortex. Decapsulation has been tried and reported ineffectual. A trial should be given to bilateral nephrotomy and temporary drainage as soon as the post-partum anuria sets in. Time should not be spent on medical treatment, which after all is but an indirect way of reducing renal tension, nor should the operation be delayed until uraemic symptoms supervene.

Anuria may set in in kidneys previously sound as well as in cases of nephritis, subacute or chronic. Besides the above post-partum infections the anuria may be started by other infections as well as by chills. Bilateral nephrotomy and temporary drainage is the surest method of re-establishing forthwith a flow of urine. The operation is not accompanied by shock nor by haemorrhage, provided that the case is not one of advanced chronic interstitial nephritis with other lesions outside the kidneys. The wounds in the loins heal before the patients are ready to get up.

(*g*) Acute septic infection of one kidney, and the right is most commonly attacked, should be treated by immediate nephrotomy. Any delay in an acute case may be fatal, or, at any rate, nephrectomy will be required. In a subacute case, in which a perinephritic abscess has already formed, it is a mistake to limit the operation to opening the abscess; the kidney should at the same time be explored and the localized focus of suppuration laid open, before the whole kidney is destroyed.

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W. G. S.

ABSTRACTS

SURGERY

Adson, A. W. Cutting the sensory root of the Gasserian ganglion for the relief of trifacial neuralgia. *Surg. Gynec. & Obst.*, 1919, **29**, 334.

Adson is a staunch upholder of the Frazier operation, but instead of performing an avulsion of the fifth root he divides it cleanly with a simple guillotine of his own devising. He lays great stress on the importance of not disturbing the ganglion more than is absolutely necessary if eye complications are to be avoided. In actual practice he only displays the hindmost end and the root. After division he pushes the proximal end of the stump back into the posterior fossa and plugs the dural opening, through which it enters the cavum Meckelii, with a muscle pad. His own observations lead him to believe that the facial paralysis which sometimes follows the operation is due to intrapontine haemorrhage due to the rough avulsion of the root. Adson, like Frazier, uses a special brain retractor carrying a small electric light, which allows of a well-lit operation field. He refers to 38 cases operated upon in the past two years, so that the Mayo Clinic seems to abound in this as in other material. G. J.

Jentzer, A. Les points de repère anatomiques et les résultats de l'anesthésie paravertébrale. [**The anatomical landmarks for, and the results of, paravertebral anaesthesia.**] *Rev. méd. de la Suisse Rom.*, 1919, **39**, 271.

In this paper Jentzer gives an account of his method of paravertebral anaesthesia, and of the 32 operations for which it has been performed (mainly by Kummer and Askanazy of Geneva). The article contains a drawing showing the average position of the spinal nerves in the intercostal spaces behind. A very simple technique is used, some five pairs of nerves being the average number injected for an abdominal operation. Those not acquainted with the method will be surprised at the range of operations performed with it. They include 8 appendicectomies, 6 cholecystectomies, 6 gastro-enterostomies, 5 partial gastrectomies, and some miscellaneous abdominal and renal operations. In 17 of the 32 cases the resulting anaesthesia was excellent; in 15 it was partially insufficient. The chief bar to success has been intra-abdominal adhesions, the separation of which has proved on the whole to be too painful a process for local anaesthesia unaided by ether. G. J.

Jentzer, A. Toutes les interventions chirurgicales sur les membres peuvent, à l'aide de points de repère précis, relever de l'anesthésie tronculaire. [**By using precise anatomical landmarks for the nerve-trunks all operations on the limbs can be performed under local anaesthesia.**] *Rev. méd. de la Suisse Rom.*, 1916, **36**, 720.

The title of Jentzer's paper tells us sufficiently well what his thesis is. He comments on the lack of information that exists even in the pioneer papers which recommended the method of anaesthetization of the nerve-trunks, as to the exact points at which the nerves are to be found. Even Braun, who first upheld the method, is silent as to the sites of injection of a large number of nerve-trunks. These omissions Jentzer makes good. The reader will do well to refer to the original for the precise points. Jentzer uses the combined Reclus and Braun methods, i.e. local infiltration plus infiltration of the nerve-trunks, but of the two the latter is infinitely the more important. In brief the method consists in an infiltration of skin, subcutaneous tissue, and sub-aponeurotic muscle tissue in circumferential manner so that the limb is surrounded by a ring of novocain solution. The deeper lying trunks are blocked by injections proximally placed. The method seems to be an admirable one and to have been skilfully and boldly used. He gives an account of thirteen operations performed with this method—3 amputations through the thigh, 1 freeing of the musculo-spiral nerve caught in callus, 3 incisions of severe phlegmons, 1 resection of the wrist, 1 reduction of dislocated ankle, 1 bone suture (humerus), and two amputations of the upper arm. One of these last two was a particularly searching test of the method. The patient was a man with a hopeless tuberculosis of the elbow. Amputation was advised and refused. The elbow-joint was therefore excised under local anaesthesia, but four days later the arm had to be amputated at the upper third. This did not suffice to stay the infection, so a disarticulation at the shoulder-joint was carried out. Later a plastic operation was done to cover the wound. All four of these operations were carried out under novocain-adrenalin anaesthesia by Jentzer's method with perfect success.

The amounts injected are large, for instance in amputating a thigh he uses 100 c.c. of $\frac{1}{2}$ per cent. novocain for the circumferential infiltration and 35 c.c. of a 3 per cent. solution for the nerve block. Without lavish use of the anaesthetizing agent major operations are impossible. G. J.

NEUROLOGY

Holmes, Gordon, and **Lister, W. T.** **Disturbances of vision from cerebral lesions, with special reference to the cortical representation of the macula.** *Brain*, 1916, **39**, 34.

Holmes, Gordon. **Disturbances of vision by cerebral lesions.** *Brit. J. Ophthalm.*, 1919, **7**, 353.

Holmes, Gordon. **The cortical localization of vision.** *Brit. M. J.*, 1919, ii, 193.

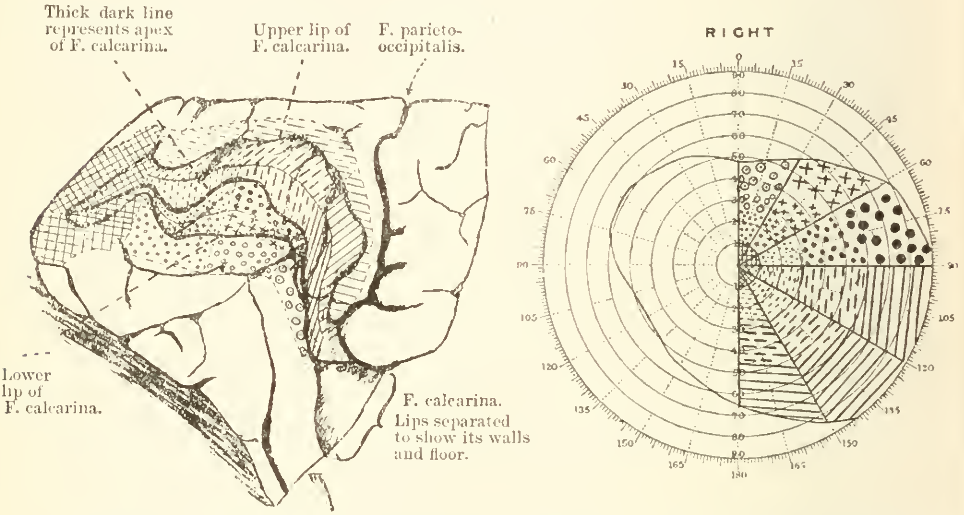
Before the appearance of this series of papers, there was little accurate information concerning the manner of representation of the different retinal segments in the visual cortex.

From a careful and extensive study of cerebral lesions involving the occipital lobes, both those which were recent and those of long standing and residual character, Gordon Holmes has been able to map out with a great probability of accuracy the topographical representation of every segment of the retina. In the majority of instances he was only able to correlate the clinical symptoms with the underlying lesion by means of cranio-cerebral measurements. Nevertheless, by careful measurement of the skull injury, by stereoscopic radiograms, and by such opportunities of direct observation of the brain as operative procedures afforded from time to time, he considers that the lesions of the visual cortex were determined with reasonable accuracy.

The observations may be summarized as follows:

(1) Complete unilateral destruction of the area striata produces complete hemianopia up to the fixation point.

(2) Injuries below the level of the calcarine fissure produce a superior quadrantic hemianopia. It appears, therefore, that the lower halves of the retinae are projected on to the lower parts of the area striata.


Thick dark line represents apex of F. calcarina.
Upper lip of F. calcarina.
F. parieto-occipitalis.
Lower lip of F. calcarina.
F. calcarina. Lips separated to show its walls and floor.
RIGHT
0
15
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135
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A diagram of the probable representation of the different portions of the visual fields in the calcarine cortex. On the left is a drawing of the mesial surface of the left occipital lobe with the lips of the calcarine fissure separated so that its walls and floor are visible. The markings on the various portions of the visual cortex which is thus exposed correspond with those shown on the chart of the right half of the field of vision. This diagram does not claim to be in any respect accurate; it is merely a schema.

(3) Injuries above the level of the calcarine fissure produce blindness of the lower homonymous quadrants, indicating that the upper halves of the retinae are represented in the dorsal part of the area striata.

(4) Bilateral injuries above the level of the calcarine fissure produce complete blindness below the fixation point.

(5) Pure superior hemianopia has not been observed, probably because a wound involving the lower parts of both visual areas must also injure the region of the torcula so severely that death results.

(6) **Central vision.** Injury of the posterior ends of the visual areas, that is, superficial injuries of the occipital poles, produces loss of central vision with integrity of peripheral vision. Hence macular vision appears to be represented in this region of the visual area. The evidence obtained from unilateral lesions confirms this view. Localized injuries in the polar

region produce paracentral scotomata, and these appear to bear the same topographical relation to the visual areas as the quadrantic visual defects.

Holmes suggests the following 'working hypothesis'. (1) The upper half of each retina is represented in the dorsal, and the lower in the ventral, part of each visual area.

(2) The centre for macular or central vision lies in the most posterior part of the visual cortex, probably on the margins and on the lateral surfaces of the occipital poles. The macula has not a bilateral representation.

(3) The centre for vision subserved by the periphery of the retinae is situated in the anterior portions of the visual areas, and the serial concentric zones of the retinae from the macula to the periphery are probably represented in this order from behind forward in the visual cortex.

(4) Those portions of the retinae adjoining their vertical axes are probably represented in the dorsal and ventral margins of the visual areas, while the retina in the neighbourhood of its horizontal axis is projected on to the walls and floor of the calcarine fissure.

(5) Severe lesions of the visual cortex produce complete blindness in the corresponding portions of the visual fields, or, if incomplete, an amblyopia, colour vision being generally lost and white objects appearing indistinct, or only more potent stimuli, as abruptly moving objects, may excite sensations.

Dealing with the escape of central vision in vascular lesions of the brain, Holmes and Lister suggest that this is due, not to bilateral representation of each macula, for their observations negative this representation, but to the anatomical arrangement of the arterial supply of the occipital poles. The occipital pole is a watershed area between the territory of both middle and posterior cerebral arteries. Hence, when one is blocked, arterial blood may be obtained from the other and the macular visual cortex escapes.

F. M. R. W.

MENDEL, K. Torsionsdystonie. (Dystonia musculorum deformans, Torsionsspasmus.) [**Torsion dystonia.**] *Monatschr. f. Psychiat. u. Neurol.*, 1919, **46**, 309.

In this monograph of over 50 pages, Mendel has collected all the recorded examples of this rare and most curious disease, and he has added two personally observed cases, bringing the total up to 33. Since its first description in 1906 by Schwalbe, cases have been reported singly and in small series in Germany and the United States by 18 observers, who have given it no less than 11 separate names. These titles being merely descriptive and without pathological basis, it is not easy to choose between them, but that of Mendel (Torsion Dystonia) is as expressive as any, and it has the merit of brevity.

A disease at once so bizarre and so obscure in nature is difficult of **definition,** but it may be summed up as a slowly progressive malady beginning in childhood, almost exclusively in the Jewish race. It is characterized by a combination of general muscular hypotonia with powerful tonic and clonic spasms of all the voluntary muscles except those supplied by the cranial nerves. These spasms give rise to uncontrollable, grotesque, and purposeless movements and to gross disorders of co-ordination; more particularly to an extraordinary gait. Other signs of organic nervous affection are wanting. Its aetiology and morbid anatomy are unknown.

Symptomatology. Its onset is insidious and is generally during the second or third five years of life, in children of both sexes. It is first noticed as a disturbance of gait. The child begins to throw one leg about when walking and tends to walk on tiptoe. Soon the other leg is affected, and the gait, and attitude when erect, become most striking. The pelvis is tilted well forward and the rump protruded behind. There is marked lordosis, and the patient struts along in a jerky manner with constant writhing movements of the rump and whole trunk ('torsion spasm'). The arms are then involved and become the seat of involuntary movements said to partake of the characters of chorea, athetosis, and paralysis agitans. All movements are clumsy and largely out of control. The head is jerked backward and forward, and the whole body is in continual motion. The face alone is free, and speech and deglutition are practically always normal. This combination of motor disorders is grossly aggravated by the attempt to walk, or by efforts to control it. It is least extravagant when the patient is recumbent, and only ceases during sleep, or narcosis.

On analysis there are said to be two main elements in the symptom-complex. (1) On passive movement all the muscles show definite hypotonus, though repeated manipulations may induce the **Tonic-clonic spasms**; In some cases tonic spasm seems to have been predominant. According to Oppenheim and Mendel it is the combination of hypotonus with these spasms which is the first essential feature of the disease. To express these variations of tone on both sides of the normal, Oppenheim has proposed the word '**dystonia**'. There is no loss of power. (2) **The involuntary movements,** which result from the spasms, Mendel describes as 'purposeless, grotesque, bizarre, clonic-tonic, unharmonious, snake-like, sinuous, unco-ordinated and stereotyped', while on the gait he is equally prodigal of adjectives, and he succeeds in conveying the impression of an exhausting malady. Walking aggravates the condition for a time. The only other objective sign is a general diminution of the tendon reflexes. There are no signs of a lesion of the pyramidal tract. There is neither sensory loss, sphincter defect, nor muscular atrophy.

As a rule the mental capacity and the emotional stability are those of normal individuals of the race. The viscera are healthy, and the hepatic and corneal changes of pseudosclerosis and progressive lenticular degeneration are not seen. No clear case has come to post mortem, so that its pathological anatomy is quite unknown. **Its course** is chronic, and it does not appear, strangely enough, to shorten life, as far as present knowledge goes. After its full development, which may take several years, it is frequently stationary, with periodical exacerbations.

Its aetiology is also obscure. There is frequently a family history of neurosis, but this is not invariable. It appears to be neither familial nor hereditary. There is nothing to indicate any infection or intoxication.

Theories as to the site of the nervous lesion, and as to the mechanism by which the symptoms are produced are as plentiful as names for the malady. Schwalbe and Ziehen, the first observers, regarded it as a neurosis, 'tonic torsion neurosis', but Oppenheim and the later observers do not agree with this view. Oppenheim regards it as due to microscopical changes in those central nervous structures governing muscle tone. Mendel thinks that it is a form of extrapyramidal motor disease, standing in an as yet indefinable relation to pseudosclerosis and progressive lenticular degeneration (vide *Medical Science*, 1919, **2**, 209). He suggests that the lesion is a degenerative or chronic inflammatory one situated in the neighbourhood of the brain-stem and corpus striatum, and involving the tonus-regulating centres: all of which is entirely speculative. **The differential diagnosis** from hysteria, chorea, double athetosis, the tics, juvenile paralysis agitans, pseudosclerosis, progressive lenticular degeneration, and myotonia is discussed at length. Under the heading of **treatment** it is mentioned that sedative drugs, orthopaedic surgical procedures, hypnosis, and psycho-analysis have all proved equally unavailing to control the severity or the course of the malady. F. M. R. W.

Nonne, M. Zum Kapitel der epidemisch auftretenden Bulbärmyelitis und Encephalitis des Hirnstammes. [**On epidemic bulbar myelitis and encephalitis of the brain-stem.**] *Deutsche Ztschr. f. Nervenh.*, 1919, **64**, 185.

Nonne describes 14 cases of lethargic encephalitis that have come under his observation during the past twelve months. They correspond with the malady described and so named by Economo in 1917, and with the accounts of Wilson, Buzzard, and others in England.

His cases were of all degrees of severity: abortive, moderately severe, and severe. They were characterized by: (1) Cranial nerve palsies, except the optic nerve. The neuro-muscular apparatus for deglutition, mastication, speech, and respiration, and the pupil and external ocular movements, as well as facial movements were impaired in varying degree. (2) Rigidity of the extremities with limitation of movement and a tendency to fixation in maintained attitudes, but no true paralysis. In the case of the face muscles this produced a mask-like facies in some instances. (3) The absence of pyramidal tract defect symptoms. Therefore the reflexes showed no change. (4) Retention of urine, requiring catheterization. (5) Profound prostration and rapid general wasting. (6) Stupor and somnolence, but no other marked psychical symptoms. (7) Fever was exceptional and there were no meningeal symptoms. The cerebrospinal fluid and the blood were normal in all.

In some of the severe cases there were residual paralytic phenomena: rigidity and fixation of the face muscles, inequality, irregularity, and reflex inactivity of the pupils.

Several of the series were associated with a recent influenza, either in the patient or in some member of his family. In some instances the clinical picture was remarkably like that of paralysis agitans, and Nonne considers that a real difficulty in diagnosis may arise. In such a case, the evolution of the encephalitis, the general prostration, and the cranial nerve palsies should help to a differentiation. He agrees that the condition has nothing in common with Heine-Medin's disease (acute polio-encephalo-myelitis).

The pathological process is a non-suppurative encephalitis affecting the basal ganglia and the nuclei of the brain-stem.

Two theoretical questions are raised by the study of this condition: that of the 'amyostatic symptom-complex' of Strümpell (vide *Medical Science*, 1919, **1**, 209), and that of the localization of sleep in a definite centre.

In Nonne's cases the rigidity was that seen in the amyostatic symptom-complex, which is quite different from that of a pyramidal lesion. This and the other disturbances of movement that may be present in lethargic encephalitis, namely tremor, athetosis, and choreiform movements, he regards as due to a disturbance, an irritation, of the nervous mechanism governing the maintenance of attitude and posture. This is localized in the basal ganglia, hence the significance of the severity with which the pathological process attacks these structures. Nonne also reviews the evidence for the localization of the functions connected with sleep in the thalamus, and suggests that involvement of this in lethargic encephalitis may be connected with the lethargy.

The description of facts contained in the paper corresponds closely with the accounts given in this country, but the theoretical considerations it contains are very largely speculative. F. M. R. W.

Williams, G. The loss of the abdominal reflexes in affections of the abdomen. *Brit. J. Surg.*, 1920, **7**, 320.

Williams finds that the abdominal reflex, in one or all of the quadrants of the abdominal wall, is often absent in certain acute abdominal affections. Thus, the right lower response may be absent in acute appendicitis, and he has found them all missing in acute renal colic. It appears, therefore, that the underlying condition need not be inflammatory, nor need an organ with a peritoneal covering be involved. It is probable that the factor common in all such examples of reflex alteration is the initial presence of pain and muscular rigidity. Williams suggests, therefore, that the mechanism is a fatigue of the reflex, cerebral in origin, due to its preliminary over-stimulation by pain.

The paper includes a summary of Rolleston's observations on loss of the abdominal reflexes in abdominal diseases, notably enteric, which were published in *Brain* in 1906. F. M. R. W.

Villaret, M., St. Giron, F., et **Capoulade, J.** Un cas de méningite alcoolique subaiguë ; constatation de l'alcool dans le liquide céphalo-rachidien. [**A case of subacute alcoholic meningitis ; alcohol in the cerebrospinal fluid.**] *Bull. et mém. Soc. méd. d. hôp. de Par.*, 1919, 3e sér., **43**, 1113.

A woman of 45, addicted to alcoholic excess, was admitted to hospital in a stuporose condition with two weeks' history of headache, increasing somnolence, loss of appetite, and constipation. On admission she was too dulled to give any connected account of herself, beyond stating that she had severe headache, frontal in situation. There were no objective signs in the nervous system except very brisk tendon jerks. While under observation she rapidly became more stuporose and developed Kernig's sign and rigidity of the neck muscles. She passed urine under her, and was at times delirious. She had a temperature of 39° C. There were no cranial nerve palsies and at no time was an extensor plantar response obtained. After about a week she began to become clearer, and improvement continued to complete recovery, so that she left hospital perfectly well at the end of four weeks. While in hospital, lumbar puncture was performed three times. The first specimen of cerebrospinal fluid obtained was slightly turbid and showed a distinct deposit on being centrifuged. No organisms were found, but there were numerous cells, 85 per cent. being polynuclear leucocytes. A week later 40 cells per c.mm. were found, but 65 per cent. were now lymphocytes. Such polynuclear cells as were seen were altered in appearance. There was also an increased albumin content. The Nicloux-Gréhant reaction revealed the presence of alcohol in the fluid.

The Wassermann in the blood was also negative, and inoculation of a guinea-pig with cerebrospinal fluid gave no result. They conclude, therefore, that syphilis and tuberculosis may be excluded, and that the diagnosis of alcoholic meningitis is justified.

In reviewing the recorded cases of meningeal reaction due to alcohol, the authors note that the occurrence of alcohol in the fluid has not been previously observed. In one case Claude found xanthochromia and massive coagulation, but no pleocytosis. F. M. R. W.

Wegeforth, P., Ayer, J. B., and Essick, C. R. The method of obtaining cerebrospinal fluid by puncture of the cisterna magna (cistern puncture). *Am. J. M. Sc.*, 1919, **157**, 789.

The authors describe the method of obtaining cerebrospinal fluid by cistern puncture. This manœuvre they have performed on animals and also on the dead and living human subject. As regards animals the method is of value because in them the ordinary lumbar puncture is usually not applicable owing to the narrowness and obliquity of the intervertebral spaces or low level of the cord. In 1,186 punctures of the occipito-atlantal ligament in the Neuro-Surgical Laboratory of Johns Hopkins Medical School the medulla was injured 10 times (0·84 per cent.). An analysis of these ten accidents showed that seven occurred during the first 527 cases and that in the later experiments there were only three such mischances. The authors believe that the chief cause of medullary injury has been anxiety to obtain fluid from all cases, without realizing that the cerebrospinal fluid may be so thick as to fail to run through the needle even when perfectly placed. Since they have realized that a dry puncture even as high as the cisterna magna may sometimes occur, they do not find medullary injury. They rely mainly on the feel of the resistance of the occipito-atlantal ligament as a guide to depth. In the cat the cisterna itself is 5 mm. deep; that is to say, the needle on puncturing the ligament is 5 mm. from the posterior surface of the medulla.

The authors have carried out a series of experiments on the human cadaver, and in two cases they performed cistern puncture on the living. The average depth of the occipito-atlantal ligament from the posterior surface of the neck in man varies from 5 to 3 cm., average 4 cm. It is therefore wiser to rely on touch, and any one skilled in lumbar puncture will, they say, experience no difficulty.

The cisterna magna is 1·5 cm. deep in man at the level of the occipito-atlantal ligament; ample room for the play of the needle-point. In a case of fractured base with streptococcal meningitis they were able to perform a most satisfactory lavage of the subdural space by means of two needles, one inserted through the occipito-atlantal ligament, the other in the usual situation in the lumbar region. They were able to wash out a quantity of pus with a stream of warm Ringer's solution at 100 mm. pressure, but the patient died 24 hours later, before the measure could be repeated. In another case, one of cerebrospinal meningitis, lumbar puncture failed to withdraw more that 5 c.c. of fluid at a time. Under light chloroform anaesthesia the cisterna magna was tapped and 40 c.c. of turbid fluid recovered, 25 c.c. of serum being injected and the patient recovering consciousness only to die the following day. At autopsy an ink injection was made into the lower lumbar region, and a complete block in the subarachnoid space demonstrated at the level of the sixth thoracic vertebra.

The authors believe that serum injected into the cisterna magna should be more efficacious owing to its more immediate relationship with the hemispheral chamber than if injected in the lumbar region. G. J.

SCHÖNFELD, W. Über Befunde in der Rückenmarksflüssigkeit bei nervengesunden Menschen. [**The cerebrospinal fluid in subjects with a healthy nervous system.**] *Deutsche Ztschr. f. Nervenh.*, 1919, **64**, 300.

Numerous and exhaustive studies of the cerebrospinal fluid in diseases of the nervous system exist, but no special and comprehensive investigation into its characters has been made in normal subjects or in those with diseases not involving the nervous system. In fact our standards of the normal have been largely worked out from the study of pathological fluids, or at least in cases of disease involving the nervous system. Our knowledge of the limits of physiological variation in the characters of the cerebrospinal fluid is still imperfect.

Working in the University Clinic for skin diseases at Wurzburg, Schönfeld has studied the question, making in all 326 lumbar punctures in 127 patients. These suffered from various skin diseases, and cases of gonorrhoea were also included, but no case of syphilis.

The points that he examined were the cell and globulin content, the effect on these of repeated lumbar punctures and the Wassermann reaction.

The cells were counted in a Fuchs-Rosenthal counting chamber, and the results correspond closely with those obtained by previous observers (cf. Fildes and Parnell, *Medical Science,* 1920, **1**, 624). From 0 to 5 cells per c.mm. is normal, from 6 to 10 on the border-line, while a content of over 10 per c.mm. may be considered definitely pathological.

The globulin content was investigated by several methods: Nonne-Apelt phase I, Weichbrodt (sublimate reaction), Pandy (carbolic acid reaction) and the Emanuel reaction (mastix reaction). The basis of these is that the appearance of a turbidity on the addition of the appropriate reagent to the cerebrospinal fluid under examination indicates a pathological increase in the globulin content. Such an increase is indicative of an organic nervous affection, almost always syphilitic in origin. The Emanuel reaction is more complex than the others, and is a colloid reaction (vide *Berl. klin. Wchnschr.* 1915, **30**, 792). With the Nonne-Apelt phase I reaction (saturation with ammonium sulphate in the cold), only 3 per cent. of the fluids examined gave a positive reaction, a result which indicates that while the test is not absolutely accurate, yet its value is considerable. The Weichbrodt and Pandy reactions gave a positive result in 69 per cent. and 59 per cent. of cases respectively, indicating that a positive reaction has no particular significance. The Emanuel reaction was only positive in 10 per cent. It seems, then, that the Nonne-Apelt reaction is the most useful.

The Wassermann reaction was uniformly negative, and this result was not modified by repeated punctures.

Repeated punctures with withdrawal of fluid produced a definite increase in the cell and globulin content, and to avoid this result Schönfeld suggests that an interval of at least ten days should be allowed to lapse between successive examinations.

It would be interesting to know whether this result obtains in cases of chronic nervous disease, such, for example, as tabes dorsalis. A fall in the cell and globulin content was one of the beneficial results claimed for the intrathecal injection of salvarsanized serum, yet it does not appear that any investigation has been made to study the effects on these changes in the fluid of simple repeated punctures. It is difficult to decide whether the results obtained by Schönfeld in this respect in normal fluids would also be found in pathological fluids. F. M. R. W.

Warwick, Margaret. Cerebral haemorrhage of the new-born. *Am. J. M. Sc.*, 1919, **158**, 95.

Warwick gives a *résumé* of the literature on the pathological anatomy of Little's disease. She points out the important rôle played by cerebral haemorrhage as a cause of death at birth. She records the results of a series of 36 autopsies conducted by herself on children born dead, or dying soon afterwards. No less than 18 (50 per cent.) had a definite haemorrhage in the dura, over the brain, or in the ventricle. There was a long labour in only two cases and forceps were applied once (6 months' baby, easy extraction). The interesting point that examination brought out was that in 8 of the babies gross haemorrhages were found elsewhere, 5 showed signs of a haemorrhagic diathesis before death by vomiting blood and by having a delayed coagulation time. It would thus appear that in a number of cases the cerebral haemorrhage is merely an incident; evidence of haemorrhagic disease of the newly born. As to the location of the haemorrhage, it extended over one hemisphere in 6 cases, over cerebrum and cerebellum in 8, and was intraventricular in 2.

Warwick classifies the causes of intracranial haemorrhage as (1) traumatic, (2) congestive-protracted labour, (3) diseased condition of child or mother. With regard to the last, the autopsy performed by Osler may be recalled where a large haemorrhage over the cortex was found in the intra-uterine seven months' foetus of a woman dead of typhoid. G. J.

Primrose, A. Cranioplasty, the value of a graft of bone, cartilage, or fascia in the closure of cranial defects caused by wounds in war. *Ann. Surg.*, 1919, **70**, 1.

Primrose records the results of 42 cases in which the cranial defects produced by war wounds and the operations for their treatment have been closed by cranioplasty. A completely satisfactory closure of the gap was obtained in 32 cases, and of these 19 were 'completely relieved of their distressing symptoms', 8 were improved, 5 were unaltered, and 2 were made worse. There were no deaths. He states that the chief symptoms referable to the defect in the skull were: a feeling of insecurity, nervousness, and fear of being struck upon the head. These subjective troubles were cured by the operation. Cerebral defect symptoms were unaffected. As for Jacksonian fits it is difficult to make a statement of positive improvement, as a sufficient time has not elapsed. It is noteworthy that headache was often completely relieved by a successful cranioplasty, though in 10 cases this desirable result was not obtained. The operation performed consists in a very thorough resection of the scar; if this produces a dural defect too large for suture, a fascial graft is taken from the thigh and applied fatty surface inward. The outer table is chiselled away around the hole in the calvarium, leaving a ledge on which to lay the transplant. This transplant consisted of rib cartilage in 27 cases, a scale of bone cut from the tibia with a chisel in 12 cases, a large piece of bone from the cadaver in 1 case, and fascial grafts in 2 more. Primrose insists that the grafts must be large enough to bridge the gap completely without a break in continuity. If this point is not attended to, failure to obtain a firm closure will probably result, owing to the mobility of the graft. The other chief cause of failure is sepsis. In one case with a huge defect a large piece of parietal bone was transplanted from the cadaver, the outer table alone being used, after boring in multiple places and thorough boiling. The result seems to have been most successful. A confirmation of this good result is furnished by the work of Gallie and Robertson of the Toronto Clinic, who have shown that there is no difference between fresh and boiled bone as a medium for grafting. In both instances the new bone is produced by vascularization from without. The fascial graft was employed in two cases. In one a cartilage graft had led to a hemiplegia with aggravation of epileptiform seizures. The cartilage was removed and a fascial graft substituted. A similar epileptic state followed a bone grafting done elsewhere. The graft was taken out and fascia introduced. Primrose makes no mention of the preliminary radiography of the head for in-driven splinters and retained missiles, nor of the examination of the cerebrospinal fluid.

It is noteworthy that three patients in this series had had silver plates inserted in this country. All had to be removed. G. J.

GOLDSCHEIDER u. BRÜCKNER. Zur Physiologie des Schmerzes. Die Sensibilität der Hornhaut des Auges. [**The physiology of pain. Corneal sensibility.**] *Berl. klin. Wchnschr.*, 1919, **65**, 1225.

von Frey concluded that the cornea was provided with sensibility to pain only, though during his investigations he found that a sense of contact was also perceived in some subjects. Nevertheless, he maintained that only pain endings were present in cornea and conjunctiva.

Goldscheider and Brückner have repeated his observations, both on the normally sensitive and on the cocainized cornea.

The present paper is a brief *résumé* of their conclusions.

They employed pointed wisps of cotton-wool, metal probes, and fine hairs to produce stimuli, and they found that below the threshold for pain constant and definite sensations of touch and of pressure could be obtained. The use of cocain appears to abolish pain sensation completely, leaving touch and pressure sense with a heightened threshold. These forms of sensation differ widely from those found on the skin in being not readily localizable, diffuse, and generally unpleasant in tone. They consider that in the normal state these forms are masked by the pain sense, and are revealed when this is abolished by the action of cocain.

These observations do not indicate whether there are specific nerve endings for these various forms of sensibility, or whether there is a single nervous mechanism. F. M. R. W.

STRAUCH, A. Hypophyseal dystrophy in hydrocephalus. *J. Am. M. Ass.*, 1919, **72**, 1731.

The patient who forms the subject of Strauch's article was a child $8\frac{10}{12}$ years old. From the outset she had headache, occasional dizziness, with polydipsia and polyuria. Soon she began to put on weight and became definitely obese, and at the same time sleepy and apathetic. The head increased in size so that it was difficult for her mother to fit her with hats. The skull in the region of the anterior fontanelle was thin, tender, and distinctly yielding on pressure. The fundi were normal when first seen, but optic neuritis appeared later. There was also ataxy of the arms of varying intensity, increased reflexes and ankle clonus, Babinski response, and involuntary micturition. Wassermann reaction negative. Blood-pressure 95 mm. Hg. 100, 150, 210 gm. of glucose were tolerated without glycosuria. Radiograms showed a greatly enlarged sella turcica and the cranial sutures widely open. The patient eventually died of broncho-pneumonia. At autopsy no tumour of the hypophysis was found, but a high grade of internal hydrocephalus, with typical flattening of the convolutions. The lateral and third ventricles were greatly dilated, and the aqueductus Sylvii closed [? by what pathological process]. The infundibulum was noted as being 12 mm. long. The hypophysis measured 7 × 11 × 16 mm., and was but slightly flattened. An account of the histological changes in this gland are given, but they were not of any very definite character. G. J.

PATHOLOGY AND BACTERIOLOGY

MAITRA, G. C. Observations on the cultural methods of gonococcus. *Indian J. M. Research*, 1919, **7**, 219.

A series of comparative tests of media for the growth of the gonococcus are recorded. First, the following media were tried for the cultivation of the gonococcus from typical acute cases. 1. Human blood agar. 2. Loeffler's blood serum. 3. Legumin agar. 4. Nasgar. 5. Ordinary agar smeared with human blood. 6. Nutrose agar.

The results were invariably negative.

Secondly 1. Loeffler's blood serum, 2. Urine-agar with 5 per cent. egg yolk were used in an atmosphere containing a reduced oxygen tension and 10 per cent. CO_2. It is shown that under these conditions both these media are equally efficient for isolating the gonococcus, but that Loeffler's blood serum is the better for subsequent subcultures.

The amount of growth can be augmented by adding 'fresh' human serum. The term 'fresh' appears to mean unheated. No comparison is made between the growth on these media and that which occurs on those media in common use for the growth of the gonococcus. G. T. W.

PLAUT, F. Die Sachs-Georgische Ausflockungsreaktion bei Syphilis mit besonderer Berücksichtigung ihrer Anwendung am Liquor. [**The Sachs-Georgi precipitation reaction with special reference to its use with the cerebrospinal fluid.**] *Ztschr. f. d. ges. Neurol. u. Psychiat.*, 1919, **52** (Orig.), 193.

A number of precipitation reactions have been introduced to avoid the difficulties associated with the Wassermann reaction (W. R). These nearly all depend upon the precipitation of the serum-globulin in the patient's serum, it being known that these globulins are more easily brought down from a syphilitic serum than from a normal serum. The serum-globulins of other diseases have, however, the same characteristic, and thus these reactions are not specific. An attempt has been made to cause a more specific precipitation of the syphilitic globulins by means of the lipoid antigen, and this was found to occur, not visibly to the eye but to the ultramicroscope. Sachs and Georgi then made use of cholesterin with the antigen, as is done in the Wassermann reaction, and much more specific results were obtained.

The author tests this method upon neurological cases. The technique is to make a 1 in 10 dilution of the patient's inactivated serum or cerebrospinal fluid with saline and a 1 in 6 dilution of the cholesterinized antigen. Two parts of serum are mixed with one part of antigen and placed for 2 hours at 37° C. and 10–12 hours at room temperature.

500 sera were tested and in 90 per cent. the results agreed with the W.R. On analysis of the syphilitic cases which disagreed, it was found that the W.R. was more often positive in old cases and much more often in congenital cases. The Sachs-Georgi reaction (S.G.) however, appeared to remain longer positive after treatment than the W.R. With regard to the apparently non-syphilitic cases (all neurological) 11 gave a positive S.G. and negative W.R., but the author considers these to be too few in number to register the reaction as non-specific.

158 cerebrospinal fluids were tested and 87 per cent. agreed. In every case the disagreement was due to a negative S.G. The S.G. did not correspond to the cell count or to the globulin or gold-sol. reactions.

In every case it is essential to use large quantities of cerebrospinal fluid, namely at least 6 times as much as serum.

The author then discusses a number of means by which the intensity of the reaction may be increased, but concludes that any increase is at the expense of the specificity. P. F.

NAGEL, K. Nachprüfung einer neuen Methode zum beschleunigten Nachweis von Tuberkelbazillen durch den Tierversuch. [**Experiments with a new method for accelerating the diagnosis of tubercle bacilli by animal injection.**] *Ztschr. f. Tuberk.*, 1919, **31**, 217.

Nagel has studied the leucocyte changes in the blood of guinea-pigs following exposure to X-rays, with a view to comparison with similar work done by American observers during the war. Very considerable leucopenia was observed. A fall from a normal count of 14,000 to about 7,000 was found to follow a single exposure to an erythema dose. Pigs treated at a single exposure with more than two erythema doses showed much greater leucopenia but died in the process. The effect of the rays reached its height after about a week, and the leucopenia affected chiefly the polynuclears, the figures throughout showing a relative lymphocytosis.

In view of Morton's claim that the diagnosis of tubercle by guinea-pig inoculation could be accelerated by exposure of the latter to X-rays, the author attempted to confirm the alleged diminution of resistance of the irradiated pig. Animals subjected to the rays were paired off with controls, and infected with virulent human bacilli. No difference in the development of the disease could be established, and the author attributes the opposite results of Morton to inadequate control experiments. In view of the recent work of Taylor and others it is regrettable that no mention is made of the histological changes in spleen and lymph glands, which promise to throw light on the functions of the lymphatic system. C. D. W.

Cooke, J. V. Complement fixation with acid-fast bacteria. *J. Infect. Dis.*, 1919, **25**, 452.

The author studies the possibility of differentiating different acid-fast bacteria by the complement fixation test. A large number of strains were collected and rabbits were immunized against them. It was found that all strains produced sera which reacted with all to a greater or less extent. Sub-groups are thus indicated. Many of the more waxy cultures gave poor fixation. It was further found that non-acid-fast bacteria, for instance *B. typhosus*, also gave fixation with acid-fast sera of high titre, and some fixation was even observed with acid-fast bacteria and antidiphtheria serum. This is thought to be due to the presence of antibodies to bacterial proteins in all high titre sera.

It was found that the serum of lepers gave a fixation with many strains of acid-fast bacteria and also with other bacteria if the titre was high. As is known, such sera may also give a positive Wassermann reaction.

The serum of tuberculous patients gives a similar fixation with acid-fast bacteria.

Throughout this work the antigens were made by precipitating suspensions of the bacteria with alcohol, drying the residue and suspending it in saline. P. F.

Gegenbauer, V. Zur Kenntnis der Ruhr des östlichen Kriegsschauplatzes. [**The dysentery of the eastern theatre of war.**] *Arch. f. Hyg.*, 1919, **88**, 219.

Dysentery was the commonest disease among Austrian troops in Galicia and the Ukraine. Most of the cases were, however, slight and entailed no loss of duty. Dysentery bacilli were found in about 90 per cent. of cases with blood and mucus in the stools, and practically all were of the Shiga variety. There appears to be variation in the effect of some of these strains upon maltose and saccharose, a variation which the author ascribes to the bacteria. The description of a Shiga bacillus which sometimes ferments saccharose is so unusual as to demand a statement as to the purity of the saccharose used. The author also describes strains of Shiga, so called because they agglutinated with Shiga serum to full titre, which fermented mannite and on further subcultivation lost their agglutinability with Shiga serum. This paper contains much that is contrary to generally accepted views. P. F.

Harris, J. E. G. Contributions to the biochemistry of pathogenic anaerobes. VIII. The biochemical comparison of micro-organisms by quantitative methods. *J. Path. & Bacteriol.*, 1919, **23**, 30.

Experimental methods are described for carrying out a comparison of the biochemical reactions of two closely allied organisms. Details are given of the apparatus for fermentation experiments and of the methods used for studying, from a quantitative standpoint, the various products of bacterial metabolism. A method is given for routine determinations of the degree of oxygen toleration of bacteria, and the suggestion is made that results should be expressed in the form of the 'aerobic index', which is defined.

Using the methods and apparatus described, a comparison is made of two anaerobes—*B. sporogenes* (Metchnikoff) and the Reading bacillus—which morphologically and in cultural reactions closely resemble each other. Full results are given of parallel fermentations on five different media, and of determinations of the degree of oxygen toleration. The organisms are shown to be remarkably similar in their biochemical behaviour, with, however, a striking difference in their powers of growing in the presence of oxygen.

The use of these methods in general investigations of the biochemical properties of bacteria is discussed, and suggestions are made for their application to aerobic organisms. J. E. G. H.

Knowles, R. The association of the bacillus of Hofmann with diphtheria in India. *Indian J. M. Research*, 1919, **7**, 203.

In this paper are reported the bacteriological findings in outbreaks of diphtheria occurring in 1917 and 1918 in a boys' school and a girls' school at Shillong, Assam.

The source of the outbreak in both cases was probably due to carrier sources. The main feature of these epidemics is held to be the abnormal incidence of Hofmann's bacillus.

This bacillus was found in 30 per cent. of cases of diphtheria and in 11 per cent. of true diphtheria bacillus carriers, whereas it was found in only 0·4 per cent. of healthy European children during the epidemic and in 5 per cent. of Indians examined in the absence of an epidemic.

It is suggested that there is a symbiotic relationship between the true Klebs-Loeffler bacillus and Hofmann's bacillus and that the variety of Hofmann's bacillus in India is associated with the rarity of diphtheria in epidemic form. G. T. W.

Gates, F. L. A method of standardizing bacterial suspensions. *J. Exper. M.*, 1920, **31**, 105.

A wire loop is gradually pushed down into a suspension of organisms in a test-tube. It is then viewed by looking down into the tube, and the depth of the loop varied till the latter disappears. This idea is elaborated and utilized to measure the opacity of bacterial suspensions. By means of a formula the measured opacity is translated in terms of the concentration bacteria per c.c. The apparatus is quite simple and details of its construction are given. For each type of organism a special constant has to be determined. Once the standards are established, suspensions of the same organism can be rapidly estimated. W. A. M. S.

Brown, H. C. Further observations on the standardization of bacterial suspensions. *Indian J. M. Research*, 1919, **7**, 238.

This paper records observations amplifying those recorded previously by the same author in association with Kirwan (Standardization of Bacterial Suspensions by Opacity. *Indian J. M. Research*, 1915, **2**, 763).

The haemocytometer method has been tried by the author, using various strains of bacteria and with Ziehl-Neelsen's carbol-fuchsin as the staining agent. Further dilutions were made with distilled water. The author finds that very widely divergent results may be obtained. With two different strains of *B. typhosus*, one strain gave normal counts while the other presented an entirely blank field, all bacilli entirely disappearing. He considers this was not due to agglutination, but is unable to say what caused their disappearance.

The author advocates that in the place of counting methods the Gravimetric method should be used as being more accurate. He suggests that the weight of the dried bacterial substance may be determined satisfactorily by observing the opacity of a suspension of the moist growth.

The estimation of opacity is carried out by comparing the suspensions with a series of standard tubes containing varying percentages of barium sulphate suspended in 1 per cent. aqueous solution of sodium citrate.

A table is published showing the relation of opacity to the weight of dried bacterial substance expressed in milligrammes per cubic centimetre of bacterial suspension, for all the commoner organisms. G. T. W.

Wade, H. W., and Manalang, C. Fungous developmental growth forms of Bacillus influenzae. *J. Exper. Med.*, 1920, **31**, 95.

In this paper the authors describe a metamorphosis of *B. influenzae* into a 'frank fungus'. They 'are confident that the cultures do not contain any contaminating organisms, as may be suggested', but do not state what are their reasons for this confidence. P. F.

Wolbach, S. B. Studies on Rocky Mountain spotted fever. *J. Med. Res.*, 1919, **41**. 1.

A whole number (196 pages with 21 plates) of the *Journal of Medical Research* is devoted to a research by Wolbach of Harvard on Rocky Mountain spotted fever, a disease first made widely known in European medical literature by the work of Wilson and Chowning in 1902. From that time till the present a great many investigators have studied this remarkable disease in all its aspects, and the work of Wolbach, besides containing a large number of original observations, is at the same time the most complete account of the whole disease, which was first located in an area restricted to the west side of Bitter Root Valley in the state of Montana. Later, it was found to invade the neighbouring states of Idaho, Nevada, Oregon, Utah, Wyoming, California, Colorado, and Washington, although not to the same degree. In each state, however, the disease is characteristically restricted to certain localities indicating definite foci of infection. Up to 1903 Wilson and Chowning obtained the histories of 126 cases in Montana with a mortality of 69 per cent. including both sexes and all ages. The heaviest incidence appears to fall on persons from 20 to 40 years old, but no age is exempt. The disease is an acute specific infective endangeitis and is characterized by onset with chill, continued fever, severe pains in the bones and muscles, headache, a macular rash, becoming petechial, and appearing first on the wrists, ankles, and back and then over the whole surface of the body. Wilson and Chowning were the first to suggest that the disease is transmitted by the wood tick of the locality and known zoologically as *Dermacentor venustus*, Banks (synonym *D. Andersoni*, Stiles) a member of the Ixodidae super-family of ticks.

From their examinations of the blood of patients Wilson and Chowning considered that the causal agent of the disease was a pyroplasm which they named *Pyroplasma hominis*. At a somewhat later period this idea was, however, refuted by Wardell Stiles. Very important facts were then elucidated by Ricketts, who speedily announced the transmission of the disease by the inoculation of the blood of human cases into monkeys and guinea-pigs, a fact admitted by all subsequent workers. Ricketts also succeeded in inducing the disease in guinea-pigs subjected to the bite of wild ticks and showed that the virus may pass through the various stages of the developing tick, and he apparently also saw the bodies which Wolbach now considers to be the actual parasitic agents which cause the disease.

The incubation period of Montana fever varies from 3 to 12 days. In experiments made on two human beings with ticks, removed from spotted fever subjects, McCalla found it to be 3 and 9 days respectively after the bite. The striking difference in the mortality of Idaho and Montana cases seems to point to the view that different types of mammalian hosts, other than man, occur. Immunity in man appears to be high, in that no instance is known of a second attack. A complete and lasting immunity also follows recovery from the disease in laboratory animals. In his elaborate memoir Wolbach gives an account of the hosts of *Dermacentor venustus* based on the observations of Hunter and Bishopp and Parker and Wells (1916), the facts of probable importance in the distribution of the virus in nature being that the larvae and nymphs of the tick feed exclusively on small animals such as ground squirrels, chipmunks, woodchucks, pine squirrels, rabbits, and mice, while the adult ticks feed chiefly on larger animals, such as horses, cattle, sheep, and occasionally pigs. In Western Montana the mountain goat would also appear to be a very important wild host.

A very extensive account of the biology of the wood tick is given by Wolbach, and it is pointed out that the entire life cycle of the tick under conditions of nature occupies two or more years. Like most other ticks, Dermacentor passes through four distinct stages, the egg, larva, nymph, and adult. Fully blood-engorged females deposit 2,000 to 4,000 eggs which hatch into six-legged larvae. These feed on small animals and require about a week for complete engorgement, after which they drop from their host, seek a sequestered nook, and in a few days become quiescent and remain so for 3 to 4 weeks, when the asexual eight-legged nymphs emerge. These pass the winter engorged or unengorged, a meal of blood being essential for further development, and again the hosts are the same small mammals on which the larvae feed. After gorging themselves with blood for about a week they leave their host and, depending on the degree of temperature, moult to sexually mature adults in from 12 to 140 days. The adult ticks feed in the spring months almost wholly on large animals like horses and cattle. After feeding for about 4 days the males seek the females, which are fertilized during the period of engorgement, when they drop from the host and find a protected spot to deposit their eggs for the new cycle of generation. It is considered probable that as adults frequently are unable to find hosts the first season a 3-year cycle is not uncommon.

Wolbach gives a detailed account of the strains of 'passage' virus with which he worked and also the methods which he employed in the breeding of ticks and their dissection.

With regard to the virus itself, Wolbach considers it as certain that it is a minute paired body often surrounded by a clear zone or halo as if encapsulated. There are, however, according to him, three morphological types, viz. (1) an extra-nuclear bacillus-like form, without chromatoid granules, relatively large and only present in ticks during the initial multiplication of the parasite; (2) relatively small rod-shaped forms with chromatoid granules, and (3) the relatively large lanceolate paired forms present in ticks and in the blood and tissues of infected mammals. He believes that this is the form in which the virus is passed between the tick and mammalian hosts, the other two types being apparently multiplicative stages. Bodies of a similar character have attained great notoriety during the last few years under the name Rickettsia (da Rocha-Lima) in connexion with typhus fever. Wolbach. however, considers the 'parasite' of Montana fever as something special and christens it *Dermacentroxenus rickettsi.*

All attempts to cultivate the virus *in vitro* have failed. A long account is given, however, of experiments to prove its specificity as the cause of Montana fever. In every instance of adult ticks proved by inoculation to be infective the parasite was found. It was not found in any tick (adult or nymph) which was non-infective. The virus was found in the ova of ticks by experiment and morphologically both in the ova and testis. It was also found in a large proportion of ticks infected as nymphs, some of these in the adult stage being proved to be infective. Control ticks, nymphs or adults, shown to be non-infective showed no parasites. Experiments carried out to determine the resistance of the virus to various injurious agents showed that it was relatively slight. Thus when dried it was apparently destroyed in about eleven hours. Citrated blood charged with virus was non-infective after 28 days. At temperatures of $-1°$ to $-\cdot3°$ C. infected citrated blood was non-infective in 9 to 12 days. A temperature of 50° C. killed the virus in 5 minutes. Emulsions of infected organs triturated with pure glycerol were found to be non-infective within one month. Whether the virus is a filter passer or not was not definitely settled as the control experiments were sometimes negative.

Wolbach concludes that the virus is not a bacterium in the ordinary sense of the term, giving as reasons, (1) its morphological sequence in infected nymphs and the presence of only one morphological type in the 'blood of mammals'; (2) its staining reactions and its appearance under dark ground illumination; (3) its extreme susceptibility to physical and chemical agents, and (4) its specificity for the peripheral vessels with the production of an identical type of lesion and disease course in all susceptible animals. The author, however, also sees difficulties in trying to place it among the protozoa.

Reference to Wolbach's memoir would be incomplete if no mention were made of the extremely minute account of the histological lesions in experimentally infected animals and in five fatal human cases. The account of the changes must prove of great value to subsequent investigators of Montana fever and allied diseases such as typhus fever and Tsutsugamushi disease (Japanese river-fever), to which it presents close resemblances. The points of resemblance and dissimilarity are carefully considered. A full bibliography and twenty-one beautiful plates completes this important and laborious investigation on a disease hitherto largely a mystery. W. B.

Nicolle, M., Debains, E., et **Césari, E.** Précipitation mutuelle des toxines et de leurs antitoxines. Application au titrage des sérums antidiphtériques et antitétaniques. [**Mutual precipitation of toxins and antitoxins. Application to the titration of antidiphtheritic and antitetanic sera.**] *Compt. rend. Acad. d. Sc.*, 1919, **169**, 1433.

Calmette and Massol showed that cobra venom mixed with antivenene develops a precipitin. In the present communication M. Nicolle and his co-workers have applied the principle of precipitin development to the titration of diphtheria and tetanus antitoxins. Toxin is prepared as usual and filtered. The filtrate is then saturated with anhydrous sodium sulphate and dried *in vacuo* over sulphuric acid. Of the dried powder 0·8 grms. are dissolved in 10 c.c. of distilled water (*A*). Gelatin to the amount of 10 per cent. is dissolved in salt solution (*B*). One part of *A* is mixed with an equal quantity of *B* which has been liquefied. After the mixture is made it is placed in the ice safe to solidify. When solid, antitoxin in varying dilutions is added and the mixture is left at room temperature for two hours when the results are read. A positive result is indicated by the appearance of a whitish disk at the junction of the gelatin and the antitoxin. The disk appears sharply in the test-tube in which the serum is diluted 1 : 50 corresponding to 300 units of antidiphtheria and 4,000 units of antitetanic serum, these being the 'normal' titres of the respective sera as sent out by the Pasteur Institute. A. D.

Besredka, A. De la vaccination contre les états typhoïdes par la voie buccale. [**Vaccination against enteric conditions** *per os.*] *Ann. de l'Inst. Pasteur*, 1919, **33**. 882.

Attention has already been directed in this publication (1919, **1**, 108) to experiments by Besredka on experimental immunization against dysentery. He pointed out that a lasting and strong degree of immunity was produced exclusively by administering cultures *per os*. The state of the culture, whether living or dead, did not matter. In the present memoir similar experiments have been carried out with *B. paratyphosus B*. Simple feeding with cultures alone did not produce immunity in this instance although success was obtained when the culture was mixed with bile and liquorice powder. In the opinion of the author the bile prepares the intestinal cells for absorption of the bacteria. The immunity thus acquired is said to be similar to that left in the disease contracted naturally. This conception is based upon the properties of the immune serum. The agglutination titre rises, by the 25th day, to 1 : 20,000 or even to 1 : 80,000, but soon diminishes to 1 : 100. The 'preventive' power of the serum follows a similar course. If now to a rabbit prepared as above another dose of virus is given two to four months later, the agglutinative titre of the serum will again ascend, whereas the 'preventive' power has completely disappeared. None the less the administration of a lethal dose of culture has now no effect. According to the author this is exactly what happens in the natural infection, and is due to the fact that the intestine is the only organ immunized and is impermeable to the virus. He concludes that the agglutinin titre is not a measure of the immunity. A. D.

Tallo, F. Ricerche sperimentali sulla latenza del micrococco di Bruce nella bile. [**Experimental researches on the latency of Bruce's micrococcus in the bile.**] *Pathologica*. 1919, **11**, 401.

Rabbits and guinea-pigs were inoculated with sublethal doses of living, fresh cultures of *Micrococcus melitensis*. In the first series of experiments $\frac{1}{4}$ of a normal loopful was used, while in the second series a whole loopful was employed. The micrococcus was found to produce a non-lethal septicaemia which, however, disappeared in 10 to 12 days. On the other hand, however, it establishes itself in the gall-bladder, and may persist there for a considerable time, and secondary invasions of the blood-stream may ensue. A. D.

Spolverini, L. Contributo allo studio dell' immuno-profilassi nella scarlattina. [**Contribution to the study of the immuno-prophylaxis of scarlet fever.**] *Policlin.*, 1919, **26**, 1081.

This paper describes the application of the complement fixation test to the diagnosis of scarlet fever. As antigen, the author uses the aqueous extract of the desquamated epithelium from patients suffering from scarlet fever. In 8 cases (children from 2–10 years) the results were positive, while in 2 cases, with renal complications, they were negative. Controls were negative. Extracts of the desquamated skin were also used as a vaccine, being injected into 10 children who previously had not had scarlet fever. Although exposed to prolonged and intimate contact with scarlet fever patients all the vaccinated escaped the infection. With the antigen prepared as above the serum of all those inoculated yielded a positive result.

A. D.

Lignières, J. Nouvelle méthode très simple pour cultiver facilement les microbes anaérobies. Les milieux semi-liquides en bactériologie. [**New and simple method for cultivating anaerobic bacteria. Semi-liquid media in bacteriology.**] *Compt. rend. Soc. de biol.*, 1919, **82**, 1091.

The simple method consists in merely using 0·25 per cent. agar instead of 1 or 2 per cent. as is ordinarily the case. The author states that anaerobes grow very luxuriantly in the weak concentration of agar. A. D.

Turro, R. Vaccination contre le virus charbonneux avec des substances non-spécifiques. [**Vaccination against the anthrax virus with non-specific substances.**] *Compt. rend. Soc. de biol.*, 1919, **82**, 1085.

White of egg beaten with 0·5 per cent. solution of ammonia bacteriolyzes anthrax bacilli at 35° to 40° C. in two to three days. When animals are injected with the fluid they are said to become resistant to the first Pasteur vaccine, while controls die. The serum of immunized animals is said to show bacteriolytic properties against the anthrax bacillus. A. D.

Rouquier, A. et **Tricoire, R.** Action de l'éther sur certains microbes pathogènes ou non-pathogènes pour l'homme. [**Action of ether on certain microbes pathogenic or non-pathogenic.**] *Compt. rend. Soc. de biol.*, 1919, **82**, 1160.

To 1 c.c. of an emulsion containing 500 to 1,000 million bacteria $\frac{1}{5}$ of its volume of pure ether is added, the tubes being sealed and maintained at room temperature. Subsequent inoculation into media shows that some microbes are very quickly killed. Thus *B. pyocyaneus*, *B. proteus*, *B. shigae*, *M. meningitidis* die in ether in 5 minutes. *B. prodigiosus* and *B. flexneri* die in an hour. *B. diphtheriae* survives up to 4 hours. *B. pneumoniae* up to 5 hours. *B. dysenteriae Y* up to 17 hours. *Streptococcus pyogenes* up to 3 days, *Staphylococcus* up to 8 days, *Pneumococcus* up to 10 days. Sporing anaerobes are not killed in 8 days. A. D.

Nicolle, Ch. et **Lebailly, Ch.** L'évolution des spirochètes de la fièvre récurrente chez le pou, telle qu'on peut la suivre sur les coupes en série de ces insectes. [**Life history of the spirochaetes of relapsing fever in the louse studied in serial sections of these insects.** *Compt. rend. Acad. d. Sc.*, 1919, **169**, 934.

Fleas were infected by sucking the blood of infected human beings or monkeys and were, thereafter, killed and prepared by the Cajal-Levaditi silver method. Study of the sections showed that the spirochaetes disappeared from the intestinal canal within 40 hours, to become extremely numerous in the lacunar system of the legs and antennae. This observation leads the authors to explain how the infection arises in nature. It is supposed that the legs and antennae break easily, thereby allowing the lacunar fluid to escape. The irritation produced by the bite calls for a scratch and the infective material may be introduced into the wound.

A. D.

Micheli, F. et **Satta, S.** Osservazioni e ricerche sulla febbre dei 3 giorni in Torino nel 1916, 1917, 1918. [**Observations and researches on the epidemic of three-day fever in Turin during 1916, 1917, and 1918.**] *Arch. per le sc. med.*, 1919, **42**, 1.

The first part of this paper deals with the differential diagnosis of influenza, pappataci fever, and dengue, the authors concluding that the epidemic in Turin was, in reality, influenza. Filtered blood from patients in the state of fever produced no symptoms in healthy subjects. Blood-cultures made during the first two days of the disease were negative. Sputa taken early in the disease showed Pfeiffer's bacillus in almost all the cases. In half of the post-mortem examinations Pfeiffer's bacillus was also isolated from the pulmonic lesions although it was never found in the pleuritic exudates. A. D.

Prym, P. Zur pathologischen Anatomie der Pilzvergiftungen. [**The pathological anatomy of poisoning by fungi.**] *Virchow's Archiv f. path. Anat.* (&c.), 1919, **226**, 229.

The author describes in considerable detail the naked eye and microscopic lesions found in seven persons who died after eating poisonous fungi—probably the deadly *Amanita phalloides* or allied species. Previous examinations by Maschka (1855), by Studer, Sahli, and Schärer (1885), by Tappeiner (1895) and by others showed that the most important lesions in man consist in intestinal ulceration with swelling of the lymphatic tissue, general congestion of all the organs with fatty degeneration in the liver and kidney; widespread haemorrhages were also constantly found. A careful analysis of all the older work will be found in the paper by W. W. Ford entitled 'The Pathology of Amanita Intoxication' (*J. Infec. Dis.*, 1908, **6**, 116).

The present author confirms most of these findings. In all cases there was marked fatty degeneration of the liver, kidney, and cardiac muscle. Haemorrhages were also constant, especially under the epicardium, on the posterior cardiac surface at the auriculo-ventricular junction, as well as in the anterior mediastinum, pleura, lung, endocardium, peritoneum, skin and areolar tissue in many parts of the body. Apart from these lesions of fatty infiltration and haemorrhage there were no characteristic changes. The author emphasizes the fact that there was no hyperplasia of the lymphoid tissue in the bowel or elsewhere, and he regards such changes as accidental. In general the findings in Amanita intoxication closely resemble those of phosphorus poisoning combined with acute yellow atrophy. The author was unable to confirm the recent assertion of Schnyder that oedema of the brain is characteristic of Amanita intoxication. W. B.

Heuch, I. C. Blodundersøgelser ved Influenza. [**Blood changes in influenza.**] *Ugesk. f. Læger*, 1919, **81**, 647–51.

Heuch has examined the blood of 30 patients suffering from influenza, of whom 10 were suffering from influenza alone, and 20 from influenzal pneumonia. In the first class there was well-defined leukopenia, most marked early in the disease. The disappearance of the leukopenia was gradual. A differential count showed considerable (relative) lymphocytosis. Aneosinophilia was also found. The relative lymphocytosis lasted longer than the leukopenia. In the second class there was considerable (absolute) leucocytosis; in 18 of the 20 cases the leucocytes numbered 10,000 or more. A differential count showed this leucocytosis to be due to an increase in the number of the polynuclear neutrophils, the number of lymphocytes being a trifle below normal. Two cases complicated by profound toxaemia, vomiting, hyperpyrexia, delirium, cyanosis and jaundice were not characterized, as was expected, by excessive leukopenia. The authors do not attach much diagnostic or prognostic importance to their findings, which may, however, help to clinch the diagnosis of pneumonia if leucocytosis is associated with recurrent bouts of fever, and the physical examination of the chest is negative. C. L.

Hansen, K. M. Erythrocyt- og Haemoglobintal hos Gamle. [**Erythrocytes and haemoglobin in old age.**] *Ugesk. f. Læger*, 1919, **81**, 1281–5.

This investigation was made in a home for the aged, and all the 40 inmates examined showed no other morbid changes than those due to age. In each of the following age-groups, 60–70, 70–80, 80–90, 90–100, there were 10 persons, 5 male and 5 female. The blood was taken from the ear without any preliminary friction, and Sahli's haemometer was used. The erythrocyte count was made with the Ellermann-Erlandsen pipettes and mixing-glass, and with Bürker's chamber graduated in the same way as the Thoma-Zeiss instrument. Neither the amount of the haemoglobin nor the number of the erythrocytes showed any appreciable divergence from the normal at younger ages. There was a trifling reduction in the percentage of haemoglobin, but when this is more than 5 to 10 per cent. the cause, in the writer's opinion, must be morbid, not physiological. C. L.

Thomsen, O. u. **Wulff, F.** Meningococinfection og Meningitis. [**Meningococcic infection and meningitis.**] *Hosp.-Tid.*, 1919, **62**, 449–64, 485–99, 513–19.

This 35-page study is an attempt to answer the questions:—Are the exanthematic forms of meningococcic infection due to certain properties belonging to definite types of micro-organism, or to temporary changes in the character of the ordinary meningococci? Are the factors determining the outbreak of exanthematic forms of the disease not directly concerned with the micro-organisms themselves, but with the general nutrition of the patient, meteorological factors, &c., or with other micro-organisms found associated with meningococci in the respiratory tract? These last hypotheses are dismissed: there is no evidence to support them. The problem is thus reduced to the alternatives;—permanent properties of a definite type of meningococcus or temporary changes. The writers favour the latter view.

The first investigations made were into the comparative frequency of meningococci among sailors, soldiers, and civilians. Of 474 men who had not previously served, and who had just been mobilized, 2·1 per cent. proved to be carriers. Of 843 other men belonging to the same category, 4·9 per cent. were carriers. In the first instance both nose and mouth were examined: in the second only the mouth. The percentage in the second instance should therefore be multiplied by $\frac{5}{3}$. bringing it up to 8·16 per cent. to make the two figures strictly comparable. Again, among 258 school-children, among whom no case of meningitis had occurred, 5·4 per cent. proved to be carriers. The writers calculate, from their own investigations and those of Fildes and Baker, that 2 to 10 per cent. of the civilian population are carriers, and as these figures are the expression of a single examination, they probably represent only half the total number of carriers. As a carrier harbours meningococci only 3 to 4 weeks as a rule, and as only about a third of the persons exposed to infection become carriers, it may be concluded that, in large towns, the overwhelming majority of the inhabitants is exposed to infection in the course of a year. But throughout Denmark only about 200 cases of the disease occur annually. On the other hand, in a small camp of about 500 men just mobilized, 10 fatal cases occurred in 9 days. The writers can account for this contrast between soldiers and civilians only on the assumption that the virulence of meningococci varies enormously under different conditions. Avirulent or only slightly virulent meningococci are transmitted from civilians to a military centre where, owing to the close intercourse of its members, facilities exist for a rapid augmentation of virulence by passage through susceptible subjects. Among civilians the virulence of these cocci is kept low, as by cultivation from one artificial medium to another. Among soldiers in confined quarters the rapid rise of virulence is analogous to that effected by passage through susceptible animals.

The writers elaborate the distinction they draw between civil and military communities in respect to the meningococcus as follows: Suppose one in 20 soldiers is susceptible to the cocci of a carrier A. Then in a camp of 400 there will be 20 soldiers who will increase the virulence of A's cocci. The remaining 380, not being susceptible to A's cocci, will not raise its virulence: they may even help to lower it. But some of these 380 will, perhaps, be susceptible to A's cocci after their virulence has been raised by passage through the 20. In this way opportunities exist for a constant augmentation of virulence. In a civilian community, the carrier A would have, on the average, to be in close contact with 20 persons if he is to convey the disease to one susceptible person. This chance is small, and meantime the virulence of the cocci is waning by transmission through comparatively unsusceptible persons. The writers believe that the maintenance of virulence of any given strain in a carrier is very variable: it may last long or quickly dwindle.

If their explanation of the rise of virulence in camps be correct, then, the writers argue, many cases should occur of infection of civilians by soldier carriers, and the number of such cases should be proportional to the degree of virulence to which the cocci have been raised. They interpret the exanthematic, notably the petechial, forms of the disease as evidence of great virulence of the cocci. Accordingly they expected to find a large proportion of exanthematic cases in civilians traceable to soldier carriers. To elucidate this point they investigated the possible source of infection among the 58 petechial cases occurring in civilians during two years in or near Copenhagen. In 30 there was evidence of potential infection by soldiers. On the other hand, among 46 non-petechial cases in civilians, there was evidence of potential infection by soldiers only in 10 cases. In the same two-year period there were 59 petechial cases among soldiers in the same neighbourhood. As there were only 58 petechial cases in the whole of the civil population, as compared with 59 among soldiers, it seems obvious that the infection travelled from soldier to civilian, and not in the reverse order. It was noted that, in the period Jan. 1917–Dec. 1918 inclusive, the petechial cases occurred within 42 weeks; in 21 weeks they occurred among both civilians and soldiers, in 11 weeks among soldiers only, and in 10 weeks among civilians only. As for the ordinary, non-petechial cases, they occurred within 47 weeks; in 9 weeks they occurred among both soldiers and civilians, in 9 weeks among soldiers only, and in 30 weeks among civilians only. Whereas half of the petechial cases occurred among soldiers, they (the soldiers) accounted for only 26 per cent. of the ordinary, non-petechial cases. These and many other figures confirm the writers' views as to the processes by which meningococci grow more virulent.

The writers record the following experiment illustrative of the great speed with which meningococci are absorbed, presumably by the blood-vessels. A mouse was given an intraperitoneal injection of 1 c.cm. of an emulsion of meningococci. Two minutes later it was killed, and a culture was made on ascites agar of 0·01 c.cm. of blood taken from the heart. Though only about five minutes had elapsed between the intraperitoneal injection and the withdrawal of blood from the heart, about 1,000 colonies of meningococci could be counted next day, and this was equivalent to about 1/3,000 part of the total quantity of meningococci injected. Leucocytes took no part in this process, for (1) the time—2 minutes—was too short, and (2) all the meningococci seen under the microscope were extra-cellular. The following experiment showed that the motion of blood in circulation is no check on the multiplication of meningococci.

Equal quantities of meningococci were added to two test-tubes containing ascites bouillon. Both were placed in a thermostat at 37° C., one motionless, the other in a holder which kept the medium in constant motion for 24 hours. The results of this experiment, frequently repeated, were invariable; the growth was most luxuriant in the shaken tube.

After pointing out that the meningococci responsible for petechial cases are abnormally virulent because the mortality is high and the proportion of adult cases is exceptionally great, the writers note that these cocci persist in the naso-pharynx of convalescents with extraordinary obstinacy. In the ordinary, non-petechial case, the meningococci rapidly disappear from the naso-pharynx, and they are absent in 80 to 90 per cent. after the 7th day of the disease. But among 22 convalescents from petechial meningitis there were 13 patients (59 per cent.) who harboured meningococci a week after the illness, whereas only in four out of 28 cases (14 per cent.) of ordinary meningitis was the examination positive after a week. In many cases the cocci in petechial cases persisted for months, and were refractory to various measures.

Hitherto the writers have failed to set up any reliable standard by which the virulence of a given strain can be judged; the reaction of mice to intraperitoneal injections does indeed vary, smaller quantities of some strains than of others proving fatal, but no differences sufficiently distinctive could be established. Proof of multiplication of meningococci in the blood of mice was also lacking, and in none of the 100 mice given an intraperitoneal injection did meningitis develop. Nor could the phagocytic response to various strains of meningococci serve as a standard by which to judge of their virulence.

The work of Gordon, of Fildes and Baker, and their classification of meningococci into groups and types is then reviewed.

The last section of this paper deals with the microscopic changes in the skin of petechial cases. The writers confirm the findings of Benda and v. Pick, but disagree in their interpretation thereof. B. and v. P. regarded the cells, stuffed with meningococci, inside the blood-vessels in sections of the skin where a petechial eruption had occurred, as leucocytes. The writers regard them as endothelial cells, detached from the lining of the small blood-vessels. Accordingly they explain the haemorrhages into the skin as the result of a sudden detachment of the endothelial cells which permits the escape of blood into the perivascular tissues. They have found that the histo-bacteriological examination of petechiae in cases terminating fatally of acute sepsis may be the only means of distinguishing between meningococcal and other forms of sepsis. The accumulation of Gram-negative cocci in the endothelial cells of the blood-vessels, and the detachment of these cells, which are found free in the lumen of the vessels, are pathognomonic. The necropsy in these doubtful cases is otherwise indecisive; the central nervous system is often intact, meningococci are not demonstrable in the cerebrospinal fluid or the brain, and serological tests (agglutination, &c.) are also incapable of establishing the differential diagnosis. Cultivation of meningococci from the blood may, indeed, clinch the diagnosis, but it is a difficult test which often fails and is usually negative after death. Hence the great importance of the histo-bacteriological examination of the skin. This should be examined as soon after death as possible. The excised portion should be fixed in a solution of formalin (1 part formalin, 8 parts water). Stronger solutions of formalin are apt to precipitate the blood in the petechiae. The paraffin sections must be thin, and the best stain is carbol-methyl-green-pyronin, the meningococci turning purple, the tissues a pale bluish-green. Further, staining according to Gram should be carried out. C. L.

Bulloch, W., Bullock, W. E., Douglas, S. R., Henry, H., McIntosh, J., O'Brien, R. A., Robertson, Muriel, and Wolf, C. G. L. Report on the anaerobic infections of wounds and the bacteriological and serological problems arising therefrom. *Medical Research Committee, Spec. Rep. Ser.*, No. 39, London, 1919.

The present Report is the conjoint work of the Anaerobe Committee formed by the Medical Research Committee in 1917, whose names appear as authors. It also contains articles by others whose names appear as indicated in the text.

The work is not only the most complete review of the subject of gas gangrene which has been published, but also contains a mass of original material which has not appeared elsewhere. It presents the bacteriology of the pathogenic anaerobes with a clarity of arrangement and accuracy which up to now has been impossible and has only become possible through the researches of the members of the Committee and their associates.

The report emphasizes the confusion which existed before the war with regard to the bacteriology of gas gangrene and ascribes this to technical difficulties in the preparation of pure cultures of anaerobes, which led to error in many of the characters with which these bacteria were endowed by their discoverers. Technical research after the outbreak of war was, however, directed towards the purity of culture, and this was much facilitated by McIntosh and Fildes's apparatus, which enabled *surface* cultures of anaerobes to be obtained with facility.

Among the numerous anaerobes to be obtained in gas gangrene, only three, probably, are endowed with any marked degree of pathogenicity to man, namely, *B. welchii*, *Vibrion septique*, and *B. oedematiens*, but *B. histolyticus* is also, in all probability, sometimes responsible.

B. welchii is the organism sometimes referred to as *B. aerogenes capsulatus* or *B. perfringens.* This bacterium has pronounced saccharolytic powers and tends to make the medium acid with the production of gas. In such cases no spores are formed, but these may be observed to a greater or less extent in rich protein media free from fermentable sugar. No digestion of meat or serum is observed, but gelatine is liquefied. The pathogenicity of *B. welchii* to animals is variable. Washed bacilli or spores never produce lesions, but broth cultures injected intramuscularly into guinea-pigs may produce a local or spreading oedema with some gas formation and death in 24 hours. The oedema is only slightly blood-stained, but the muscles are pink and friable. No putrefactive odour occurs. The bacteria may be found without spores in all organs of the body.

No agglutinins to *B. welchii* have been demonstrated.

Vibrion septique has hitherto been understood to be different to *B. oedematis maligni*, but the report, following McIntosh, now classes the latter with the former. The alleged point of difference, namely, the putrid digestion of proteins by *B. oedematis maligni* is looked upon by the Committee as a fallacious observation due to impure cultures.

Vibrion septique, unlike *B. welchii*, is a motile easily sporing bacillus. In surface culture it has a great tendency to grow in a continuous film, while in 'shake' cultures it produces delicate branching colonies. This bacillus also has considerable saccharolytic properties, but to a less marked degree than *B. welchii.* It does not ferment saccharose as does the latter.

There is no putrid digestion of proteins, but gelatine is liquefied. Guinea-pigs inoculated with a sufficient quantity of a broth culture never recover. A quantity sufficient to infect is sufficient to kill. There is a marked blood-stained oedema with pronounced gas formation, but no putrid odour.

Upon the peritoneal surfaces the long snake-like masses of bacteria from which the organism derives its name are found. These masses are important points of distinction between *Vibrion septique* and *B. chauvoei* (bacillus of 'Black Quarter'—Rauschbrand) which has been confused with it.

Agglutinins are readily produced in rabbits, and, by using monovalent sera, different serological races may be demonstrated among these bacilli.

The third bacillus which is capable of causing gas gangrene is *B. oedematiens*, a new variety discovered by Weinberg and Séguin, during the war, but probably identical with a bacillus described by Novy in 1894. It is a motile organism when examined under strict anaerobic conditions and very readily forms spores. Surface cultures tend to coalesce and form films. The saccharolytic action of this baccillus is less marked than of those already noted; it ferments neither saccharose nor lactose. There is no putrefaction of media.

Animals succumb to broth cultures of *B. oedematiens* with the formation of a colourless oedema practically without gas formation. The bacilli are sparse except at the point of inoculation.

Agglutinins can be produced against *B. oedematiens*, but these affect only the homologous strain.

B. histolyticus is also a new variety described by Weinberg and Séguin. It differs from the more pathogenic varieties in having a marked proteolytic action; meat is digested and serum liquefied. Different strains vary very much in pathogenicity, the characteristic lesion being a more or less pronounced digestion and liquefaction of the soft parts in the neighbourhood of the inoculation.

Interpolated into this section, which deals with those pathogenic anaerobes which are capable of causing gas gangrene, is an account of the bacteriology of other anaerobes which, although incapable of causing gas gangrene, have been studied anew during the war. Among these may be mentioned *B. botulinus* and *B. tetani*, many of the stock strains of which were found by modern methods to be impure. W. J. Tulloch adds a chapter on recent tetanus researches, including his differentiation of serological types and a discussion of the practical bearing of this discovery upon the treatment of tetanus.

A number of bacteria are described which are themselves non-pathogenic, but which are thought to be auxiliary to the action of the pathogenic anaerobes already discussed. The best known is the common *B. sporogenes*. The Report notices at length the 'clinging and pervasive' characters of this bacterium, familiar to all workers on the subject, which renders the preparation of pure cultures of many anaerobes so difficult. Other non-pathogenic varieties are described, most of which are the discoveries of McIntosh; Douglas, Fleming, and Colebrook; Henry; and Stoddard.

Dealing with the biological classification of anaerobes, the Report clears up some of the misconceptions which have arisen with regard to the applicability of agglutination. On the whole they regard this test as ultraspecific and liable to differentiate sub-groups in species, which leads to an 'unwarrantable multiplication of types', unwarrantable in the sense that all members of a species appear to form the same toxin which is neutralized by the same antitoxin.

The biochemistry of the anaerobes is touched upon in a manner which indicates a wide field of research in its infancy. Wolf and his co-workers are responsible for much of the advance in this direction. Up to the war the study of the chemistry of anaerobic growth was almost exclusively confined to the use of impure cultures, and therefore requires revision.

The nature of the intoxication produced, apart from that due to toxins, is discussed. It is thought improbable that either an alkalosis or an acidosis is an important factor.

In the section dealing with experimental gas gangrene it is explained that the non-pathogenic anaerobes, when injected into an animal, cause at the most a local abscess in which the bacteria are destroyed by lysis and phagocytosis; indeed the same may be said of the pathogenic varieties if these are injected free from toxin. The toxin, however, acts as an aggressin and inhibits the destructive power of the animal, allowing the bacteria to spread and cause an intoxication. Bullock (now Gye) and Cramer showed that ionizable calcium salts have the same action, and also certain colloidal substances, in particular silicic acid. The Report suggests that this factor, namely, the contamination of the wound with earth containing soluble calcium salts, is the most important in determining the onset of a local abscess or a spreading gas gangrene. The work of the same authors is also favoured by the Report as an explanation of the cause of death in gas gangrene. This is described as due to exhaustion or paralysis of the suprarenal glands and the consequent absence of adrenalin. It is brought about by the great production of acid by the bacteria acting upon the suprarenal glands in conjunction with haemorrhage and cold, a conclusion which is, however, at variance with that expressed in the biochemical section.

Fleming contributes two interesting sections upon the relation of aerobic bacteria to gas gangrene. He shows that these may have a very important effect in determining an anaerobic invasion either by exhausting the oxygen, and thus facilitating anaerobic growth, or by altering the serous medium to a condition which allows the multiplication of the 'sero-saprophytic' anaerobes.

The following sections deal with the practical technical methods for isolating and growing different varieties, namely, suitable methods for excluding oxygen and selective media. It may be mentioned that Tulloch, who isolated large numbers of tetanus strains, made use of media rendered inimical to *B. sporogenes* and other bacteria by being allowed to putrefy and become 'exhausted' to such bacteria.

The occurrence of specific toxins produced by the pathogenic anaerobes has been mentioned already. The Report contains much new information of a technical character upon these poisons and the practical methods for manufacturing antisera. *B. welchii* produces a true exotoxin which has a marked 'aggressive' and necrotic action on the tissues, but when compared with tetanus or diphtheria toxin it is poisonous only in large doses. Both effects can be neutralized by an antitoxin prepared by inoculation of an animal with toxin. The antitoxin will confer a passive immunity against the toxin and may be used therapeutically after the intoxication has started.

The toxin of *Vibrion septique* has very little effect upon subcutaneous or intravenous inoculation. Its action is best shown by the intravenous route. Its antitoxin differs markedly from *B. welchii* antitoxin in being unable to neutralize the toxin after this has been inoculated. The effect of the toxin upon rabbits is much more acute than with *B. welchii.* It is convulsive rather than paralytic, and the animal usually dies in a minute or two.

B. oedematiens toxin is chiefly characterized by the production of massive oedema locally.

The preparation of large quantities of these three antitoxins for use in the war was entrusted to the Wellcome Research Laboratories. They were made up with and administered with the routine antitetanus injection, but these sera only became available when the war was drawing to an end. An analysis of their practical value is difficult, owing to the small numbers treated, but the Report holds that the results were good beyond expectation. The antitoxin should be effective against *B. welchii, Vibrion septique, B. oedematiens,* and *B. fallax.* It should be given early in large doses. The prophylactic administration of such a serum should have great practical value.

The Report contains a chapter by J. Fraser upon the clinical aspects of gas gangrene and an appendix on the histo-pathology by Kettle. It is completed by a bibliography, compiled by W. Bulloch, which is exhaustive, and indispensable to all future workers upon anaerobic organisms.

A large number of admirable coloured and half-tone plates are included.

P. F.

BIOCHEMISTRY

Reach, F. Der Schliessmuskel des Ductus choledocus in funktioneller Beziehung. [**The functional relations of the sphincter of the bile-duct.**] *Arch. f. exper. Path. u. Pharmakol.*, 1919, **85**, 178.

The pharmacological control of the sphincter of the bile-duct would be of considerable clinical value.

The rate of flow of liquid under a constant head of pressure was measured in guinea-pigs. Distension of the stomach with air, acid, alkali, or neutral solution caused closure of the sphincter whilst emptying of the stomach caused opening of the same.

Amongst drugs, morphin caused closure, whilst papaverin and scopolamin caused opening.

H. E. R.

Hanzlik, P. S. and **Weidenthal, C. M.** **The haemostatic properties of thromboplastic agents under different conditions.** *J. Pharmacol. & Exper. Therap.*, 1912, **14**, 189.

Various agents were tested on superficial haemorrhage from the pads of dogs' feet. Thromboplastic agents produce variable and limited results, but these agree with their power to accelerate coagulation *in vitro.*

Haemorrhage from a cut femoral artery or from wounds in bone or in liver give unsatisfactory results. Haemorrhage *per se* shortens the coagulation time of dogs' blood.

In a case of haemophilia 4 grm. of kephalin appeared to stop an intestinal haemorrhage, but a previous haemorrhage in the same patient had stopped spontaneously.

The substances tested showed a decreasing power of aiding coagulation in this order: thromboplastins, kephalin, saline, coagulen and haemostatic serum.

H. E. R.

Gasser, H. S., Erlanger, J., and **Meek, W. J. Studies in secondary traumatic shock. IV. The blood-volume changes and the effect of gum acacia on their development.** *Am. J. Physiol.*, 1919, **50**, 31.

Gasser, H. S. and **Erlanger, J.** (1). **Studies in secondary traumatic shock. V. Restoration of the plasma volume and of the alkali reserve.** *Am. J. Physiol.*, 1919, **50**. 104.

Erlanger, J. and **Gasser, H. S.** (2). **Studies in secondary traumatic shock. VI. Statistical study of the treatment of measured trauma with solutions of gum acacia and crystalloids.** *Am. J. Physiol.*, 1919, **50**, 119.

Erlanger, J. and **Gasser, H. S.** (3). **Studies in secondary traumatic shock. VII. Note on the action of hypertonic gum acacia and glucose after haemorrhage.** *Am. J. Physiol.*, 1919, **50**, 148.

Erlanger, J. and **Gasser, H. S.** (4). **Hypertonic gum acacia and glucose in the treatment of secondary traumatic shock.** *Ann. Surg.*, 1919, **69**, 389.

These papers contain a very detailed account and discussion of an extended series of experiments on shock which was induced experimentally in various ways, namely, injection of large doses of adrenin, clamping the aorta, clamping the vena cava and manipulating the intestine. The conclusions arrived at in this series of papers may be summarized as follows: Shock is always associated with a concentration of the blood and a loss of volume. But the loss in volume can not always be accounted for by the concentration of the blood; the blood unaccounted for must therefore be stagnant somewhere. The factors which are responsible for the loss of volume are analysed and held to be:

Transudation of plasma alone.
Jamming of the corpuscles in the capillaries and vessels as the result of transudation.
Absolute stasis in some parts of the vascular system.
Haemorrhages into tissues, especially the lumen of the intestine.
Dilatation of the capillaries and small veins, and consequent slowing of the circulation.

By the injection of a suitable combination of gum acacia solution with glucose or sodium bicarbonate, the blood-volume, blood-pressure, and reserve alkali can be brought to normal and held there for the usual duration of an experiment. Yet many of these animals die within 24 hours. Similarly the injection of a few c.c. of strong gum acacia solution, preliminary to the experimental measure designed to produce shock, will prevent the subsequent transudation of plasma, so that the loss of blood-volume is diminished. Yet such animals were no more difficult to put into shock than their controls. The authors conclude therefore that the alterations in blood-volume and blood-pressure do not constitute the primary cause of death from shock, but are merely symptoms of some more fundamental process.

By applying a standard trauma in producing shock, the authors have been able to compare the efficacy of various combinations of gum and glucose or sodium bicarbonate. If no treatment was given after the standard trauma (partial occlusion of the inferior vena cava for 2¼ hours) 48 per cent. of the animals died within 48 hours. Of the various combinations tried, the only effective combination was a 'hypertonic gum-glucose solution' (25 per cent. gum in 18 per cent. glucose, dose 5 c.c. per kilo of body weight and per hour). After treatment with this solution only 24 per cent. of the shocked animals died within 48 hours.

The solution itself is innocuous and severe haemorrhage does not contra-indicate its use.

The details of the preparation of the solution and of the technique of injection are given in the paper in the *Annals of Surgery*, which also contains the clinical evidence. W. C.

Mann, F. C. Experimental surgical shock. V. The treatment of the condition of low blood-pressure which follows exposure of the abdominal viscera. *Am. J. Physiol.*, 1919, **50**, 86.

Shock was produced experimentally in dogs under ether by exposing and gently manipulating the intestine. When the blood-pressure had fallen to a certain level and remained there the viscera were returned to the abdominal cavity; the wound closed and the various therapeutic measures applied. The efficacy of various measures was then tested.

General measures. The application of heat is the most important one. The value of posture (keeping the head down) could not be corroborated experimentally. Rebreathing was not found to be of importance.

Drugs. None of the drugs usually employed (Stimulants, vaso-constrictors) were found to be very effective.

Restoration of fluid volume. The best results were obtained by the injection of fluid media. None of the artificial solutions gave as good results as the use of blood or blood serum. Solutions of gum acacia or gelatin come next. But the results obtained were variable and sometimes—as the author puts it—'disastrous'. The combination which gave the best result in his hands was 6 per cent. gum acacia, 10 per cent. glucose and 1 per cent sodium sulphate. W. C.

Falta, W. u. Richter-Quittner, M. Über die Verteilung des Zuckers, der Chloride und der Reststickstoffkörper auf Plasma und Körperchen im strömenden Blute. [**Upon the distribution of sugar, chloride, and of the non-protein nitrogen in the plasma and corpuscles in the circulation.**] *Biochem. Ztschr.*, 1919, **101**, 148.

The authors draw attention to the lack of agreement between the various experimenters as to the amount of sugar, &c., normally held by the corpuscles of the blood of man and other animals. They publish the results of experiments upon 36 cases, including the following animals as well as man, viz. horse, cow, rabbit, and goose. From these they conclude that in the circulating blood of man and of the animals mentioned the sugar, free and bound chloride and the nitrogen remainder (non-protein N-containing bodies) are to be found in the plasma alone. The blood corpuscles are free of these substances both under fasting conditions and when sugar, chlorides, or proteins are added to the diet. They find that the content of these substances in the whole blood and plasma only is sufficiently reliable to admit of a calculation of the blood corpuscle volume under ordinary conditions, in good agreement with a haematocrit estimation. In the pathological conditions of the hyperglycaemia of diabetes, the increase of non-protein amino bodies in forms of kidney insufficiency or pneumonia, or of hyperchloraemia in kidney insufficiency, these substances are still found completely in the plasma. They found, however, in certain states of nephritis (and kidney disease) the non-protein nitrogen as well as the free chloride in part in the corpuscles.

They attribute the differences between their experiments and those of other workers to their method of experiment. They consider that the addition of Na oxalate or Na fluoride to the blood plasma to prevent clotting is liable to alter the permeability of the blood corpuscles and so lead to the passage of substances through the blood corpuscle wall after withdrawal of the sample. They think that it is important not to let the blood stand, and above all not to cool it in ice. They therefore avoid the cooling by treating their samples with hirudin, and centrifuging in a rapid machine at once.

R. A. P.

Folin, Otto and **Wu, Hsien. A system of blood analysis.** *J. Biol. Chem.*, 1919, **38**, 81.

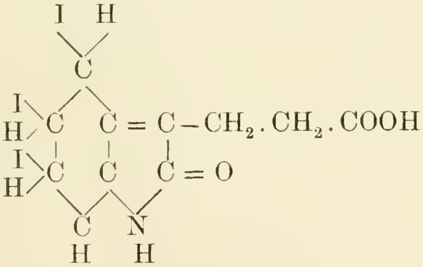
The determination of non-protein nitrogen, urea, creatinin, creatin, uric acid, and sugar in the filtrate from 10 c.c. of blood. R. A. P.

Butcher, R. Adams. Vitamine studies. IV. Antineuritic properties of certain physiological stimulants. *J. Biol. Chem.*, 1919, **39**, 63.

The attempts to determine the real nature of a vitamine are still proceeding. Birds with polyneuritis were fed with thyroxin, pilocarpin and tethalin with some evidence of improvement. R. A. P.

Kendall, E. C. Iodine compound in thyroid. *J. Biol. Chem.*, 1919, **39**, 125.

An account of the isolation of thyroxin, the active principle of the thyroid gland, being 4, 5, 6 tri-hydro, 4, 5, 6 tri-iodo, 2 oxy beta indole propionic acid.



The number of factors influencing the yield have been shown to be very large, in fact, it took four years of hard experiment to repeat the original lucky isolation. R. A. P.

Jackson, C. M. and **Stewart, C. A. Effect of inanition in the young upon the size of the body and organs of the rat.** *J. Exper. Zool.*, 1920, **30**, 1. (*Physiol. Abstracts*, 1920, **4**, 493.)

Groups were under-fed from birth to 3 to 10 weeks of age and from 3 weeks to nearly 1 year. Thereupon they were fully re-fed. They grew variably, but were permanently stunted. Perfect recovery was found after under-feeding from 3–10 weeks. The effect thus varies according to the age and the extent of the under-feeding. Early starvation apparently retards the later growth process of the body as a whole. C. G. L. W.

Arbuzow, K. A. The influence of morphin and heroin on the isolated heart of carnivorous and herbivorous animals. *Dissertation, Kharkov,* 1917. (*Physiol. Abstracts,* 1919, **4**, 404.)

The isolated heart of the rabbit is least sensitive to these drugs, the heart of the dog is most sensitive.

Weak solutions of morphin (1 : 3,000–5,000) evoke at first a transitory excitation of a rabbit's heart, sometimes of the cat's, never of the dog's. This excitation is followed by an inhibition which begins in dogs immediately after the administration of the drug. It consists in a slowing of the rhythm and in a lowering of the height of the contraction. Strong solutions of morphin (1 : 1,000–1 : 2,000) produce inhibition in all three species. Heroin affects the heart more strongly than morphin. Solutions of heroin 1:5,000–1 : 7,000 are equivalent to those of morphin 1 : 1,000–1 : 5,000. The effect of heroin begins much earlier than that of morphin; in contrast to morphin it inhibits at once the activity of the heart in rabbits and cats. Adaptation to poisons is more clearly shown with morphin than with heroin.

C. G. L. W.

Emerson, C. The preservative for Wassermann reagents. *J. Lab. and Clin. M.,* 1919, **5**, 62.

1. Antigen is best used as an alcoholic extract.
2. Red cells are kept in cold storage after being washed with a salt solution $1\frac{1}{2}$ times as strong as normal saline solution.
3. Ambocepter is preserved with chloroform.
4. Suspected and control sera are treated with chloroform.

C. G. L. W.

Jackson, D. E. and Mills, C. A. An experimental investigation of the pharmacologic properties of the active principle of commercial pituitary extracts and of the comparative action of histamin. *J. Lab. and Clin. M.,* 1919, **5**, 1.

Jackson had previously observed a difference in the action of pituitrin and histamin on the bronchioles of the dog. Later the U. S. Pharmacopoeia adopted histamin as a standard for testing commercial samples of the infundibular portion of the pituitary gland. The authors have examined various commercial preparations of pituitary extracts in order to discover if part of the action is due to histamin.

Experiments were made with histamin, tyramin, on the contraction of the bronchiole blood-pressure and uterine volume. They summarize the results of their experiments as follows:

1. The true active principle of the posterior portion of the pituitary gland is a simple body of the sympatho-metic amine type which, in the dog, produces contraction of the uterus and fails to contract the bronchi.
2. This is probably due to an action of the substance on certain nervous elements and is not a direct muscular action.
3. Certain commercial preparations of the pituitary gland apparently contain small and variable proportions of histamin sufficiently great to exert some therapeutic action, but it is not a necessary constituent of first class preparations of the gland.
4. It is probable that the action of histamin on the bronchiole of spinal

dogs can be used as a commercial test for the presence of small amounts of this substance in ordinary preparations of the gland.

5. It is probable that there are obvious clinical advantages in favour of pituitrin rather than of the intense broncho-constricting and blood-pressure lowering histamin for obstetrical uses. Very small amounts of histamin would not be of serious disadvantage in gland preparations.

C. G. L. W.

McCarrison, R. The genesis of oedema in beri-beri. *Proc. Roy. Soc.* 1920, B. **91**, 103.

In avian beri-beri oedema was found associated with enlargement of the adrenal glands. The adrenalin content of the hypertrophied adrenals, as estimated by chemical methods, was found to be slightly less per gramme of gland than in health or in so-called dry beri-beri. In spite of this the total quantity of adrenalin greatly exceeded the amount found in healthy animals: this was specially so in cases of wet beri-beri. From these observations it is concluded that a greatly increased production of adrenalin follows a deficiency of certain accessory food factors and that this excessive production of adrenalin is connected with the production of oedema found in this order of cases. The possibility of excess of adrenalin being a possible factor in the causation of oedema in general must therefore be considered.

H. M.

Young, W. J., Breinl, A., Harris, J. J., and **Osborne, W. A. Effects of exercise and humid heat upon pulse rate, blood-pressure, body temperature, and blood concentration.** *Proc. Roy. Soc.*, 1920, B. **91**, 111.

An increase in the pulse rate and in blood-pressure followed vigorous exercise of short duration. This was accompanied by an increase of the CO_2 percentage of the alveolar air. Both the pulse rate and blood-pressure very quickly fell to normal after discontinuance of the exercise. The alveolar air at rest showed a lower CO_2 content in inhabitants of tropical Queensland than the European average.

Prolonged exercise led to a rapid increase in the pulse rate and temperature at first, this increase becoming more gradual afterwards. Sometimes the profuse sweating, ultimately induced, caused the temperature to fall below normal. Prolonged exercise had little effect on the alveolar air. The body temperature continued to rise slowly during the exercise and, considering the light nature of the exercise, the rise in temperature was considerable. Blood estimations indicated that the large loss of water from the body following prolonged exercise did not cause any appreciable concentration of the blood plasma; this water therefore must have been derived from other sources in the organism than the blood plasma. In hot room experiments there was a more gradual rise of pulse rate and body temperature at first, but a quicker rise took place afterwards.

These results indicate that both exercise and humid heat play a part in producing a rise in blood-pressure, pulse rate, and body temperature. The degree of rise is, however, controlled by atmospheric conditions which influence the rate of cooling of the body.

H. M.

Funk, C. Action of substances influencing the carbohydrate metabolism in experimental beri-beri. *J. Physiol.*, 1919, **53**, 247.

On the assumption that the anti-beri-beri vitamine plays an important part in carbohydrate metabolism, experiments were carried out on pigeons to determine the effects of substances known to influence this metabolism—glucose, phloridzin, adrenalin, pituitrin, thyroid, and parathyroid glands. These substances were given to pigeons fed on a normal diet and to birds fed on polished rice. The effect of their action was sought for in a study of the blood-sugar concentration, the total liver glycogen and the amino-acid content of the blood: their influence on the onset of beri-beri, duration of life and loss of body weight in pigeons fed on polished rice was also investigated. Glucose is said to have produced practically a disappearance of glycogen and a diminution of blood sugar both in controls on normal diet and in pigeons fed on polished rice. Phloridzin increased the glycogen and sugar in the controls, decreased the glycogen and slightly increased the sugar in the rice series; this substance also seemed to hasten the onset of beri-beri and increase the loss in weight. Adrenalin and pituitrin had little effect, but thyroid gland produced a considerable sugar increase in the rice series with a disappearance of glycogen and increased amino-nitrogen in both series. Many of the birds receiving thyroid gland died before the symptoms of beri-beri appeared. Parathyroids were quite different in their action, producing an increased glycogen content with moderate increase in blood sugar and decrease of amino-nitrogen. H. M.

Fleming, G. B. Carbohydrate metabolism in ducks. *J. Physiol.*, 1919, **53**, 236.

Diet influences the respiratory exchange in ducks just as in mammals. The injection of adrenalin or removal of the pancreas produces hyperglycaemia. There is a rise in the respiratory quotient after the injection of adrenalin in the fasting animal, but it falls quickly, though hyperglycaemia still persists. This, perhaps, suggests that adrenalin causes inhibition of the internal secretion of the pancreas. In pancreatic diabetes the evidence indicates a loss of power on the part of the tissues to utilize glucose, so that the sole metabolic error does not appear to be connected with the liver. H. M.

Kozawa, S. Note on the permeability of red corpuscles for glucoses and glucosamine. *J. Physiol.*, 1919, **53**, 264.

In man the red blood corpuscles are easily permeable to blood sugar, while in the dog they appear to be slightly permeable and in the rabbit impermeable. There is no evidence that the sugar content of the red corpuscles is ever greater than that of the medium in which they are immersed. Human red corpuscles are permeable to glucosamine, while those of the rabbit, dog, and horse are impermeable. H. M.

Burridge, W. A simple definite test for ascertaining the existence of functional cardiac calcium. *J. Physiol.*, 1919, **53**, 269.

When hearts are stopped in diastole as the result of treatment with oxalates or citrates they show a definite change in the manner in which they react to 5 per cent. potassium chloride solution. While, in normal hearts, this strength of potassium chloride elicits a maximum ventricular contraction, no contraction takes place in hearts rendered quiescent by oxalates or citrates. Since there is evidence that this change is dependent on a loss of the normal functioning calcium of the cardiac tissue, it is argued that a heart which shows this changed reaction is devoid of functional cardiac calcium. This changed reaction to potassium chloride has never been observed in a beating heart, hence it is concluded that every beating heart must contain functional calcium. H. M.

Hyatt, E. G. The action of alcohol on the heart and respiration. *J. Lab. and Clin. M.*, 1919, **5**, 56.

Experiments on the spinal animal after the effects of the preliminary anaesthetic have passed off.

Administered by the mouth, alcohol stimulates the heart and respiration.

Given intravenously in quantities sufficient to kill in 1–2 hours, there is no effect until just before death, when a rapid fall of blood-pressure takes place.

Given rapidly intravenously there is a sudden fall followed by an immediate return to the normal.

When introduced by tube into the stomach there is no effect.

C. G. L. W.

Burge, W. E. The effect of adrenalin on the blood catalase. *J. Lab. and Clin. M.*, 1919, **5**, 59.

The injection of adrenalin increases the blood catalase, as the former has been shown to be excreted in greater amount during combat, and as increased catalase is connected with increased oxidation, it is possible that adrenalin stimulates catalase production in order to provide the oxidative mechanism necessary for great muscular exertion. C. G. L. W.

Kellaway, C. H. The hyperglycaemia of asphyxia and the part played therein by the suprarenals. *J. Physiol.*, 1919, **53**, 210.

The hyperglycaemia and accelerated secretion of adrenalin produced by asphyxia are caused mainly by lack of oxygen, excess of CO_2 playing at most but a minor part. In anoxaemia of ordinary severity both effects are due to action on the central nervous system through impulses carried along the splanchnic nerves. In severe anoxaemia, even when the splanchnics are cut, both may be produced by peripheral action. The hyperglycaemia is only partially dependent on the accelerated output of adrenalin. H. M.

Bayliss, W. M. The neutrality of the blood. *J. Physiol.*, 1919, **53**, 162.

The hydrogen-ion concentration of the plasma is not increased by the intravenous injection of acid in sufficient quantity to neutralize half the bicarbonate of the blood. This result is brought about chiefly by increased pulmonary ventilation and consequent decrease of the CO_2 in the blood, since, in short experiments, renal and liver compensatory mechanisms play little part.

Alkali when injected is not so readily neutralized, the chief agent in this case being excretion by the kidneys.

The plasma proteins play no perceptible part in maintaining neutrality in the living organism. No evidence was obtained that any CO_2 is carried to the lungs from the tissues by the proteins or sodium bicarbonate of the plasma, and it is therefore assumed that under normal conditions the sole function of the sodium bicarbonate of the blood is to regulate hydrogen-ion concentration, while the only function of the protein is to preserve a colloidal osmotic pressure and a moderate degree of viscosity of the plasma. A method for the determination of the hydrogen-ion concentration of the blood by means of indicators is described. H. M.

Haldane, J. S., Kellas, A. M., and **Kennaway, E. L. Experiments on acclimatization to reduced atmospheric pressure.** *J. Physiol.*, 1919, **53**, 181.

A description of the effects produced in different persons by different degrees of reduction of atmospheric pressure and of reduction of oxygen percentage in the air breathed.

During the anoxaemia the amount of acid excreted by the kidneys is markedly diminished; this is accompanied by a less marked diminution in the ammonia concentration. Partial acclimatization to reduced atmospheric pressure was obtained, but this depended almost entirely on increased inward secretion of oxygen by the lung epithelium. The conclusion is drawn that the supposed slight acidosis of acclimatization is really an alkalosis brought about by the increased breathing resulting from the anoxaemia. H. M.

Honeyman, T. J. The thymus and tetany. *J. Physiol.*, 1919, **53**, 207.

There is no evidence that the thymus contains or secretes any substance capable of producing tetany, or of modifying in any way the onset of symptoms caused by the removal of the parathyroids in the guinea-pig. H. M.

Valenti, A. Contribution expérimentale à la connaissance de la signification physiologique de l'inosite. [**Experiments on the physiological significance of inosite.**] *Arch. ital. de biol.*, 1919, **69**, 215.

With a view to determining whether inosite combined with phosphoric acid in the organism and thus facilitated the assimilation of inorganic phosphates, the author administered inosite and di-sodium phosphate to dogs. Estimations of the phosphoric acid in the urine and faeces during experimental and control periods appeared to indicate that a small portion of the additional phosphorus was retained in the presence of inosite. H. M.

Cow, D. Histamin and pituitary extract. *J. Pharmacol. and Exper. Therap.*, 1919, **14**, 275.

On the uterus of the mouse histamin causes relaxation whilst pituitary extract causes increased tone; hence the two substances are not identical. H. E. R.

Hanzlik, P. S., Howard, T. K., and **Fetterman, J. Anaphylactoid phenomena from thromboplastic agents.** *J. Pharmacol. and Exper. Therap.*, 1919, **14**, 229.

The injection of haemostatic solutions containing protein is undesirable because of the danger of anaphylaxis; thus thromboplastin and haemostatic serum produce anaphylaxis, coagulen causes more pronounced anaphylaxis, but kephalin is preferable because it does not produce anaphylaxis.
H. E. R.

Sollmann, T. Experiments with carvacrol. *J. Pharmacol. and Exper. Therap.*, 1919, **14**, 251.

Carvacrol is an isomer of thymol which can be produced at low cost from spruce-turpentine; it forms suspensions with water. It has a high toxicity for earthworms and in dogs is effective against ascarids, but dogs proved to be unsatisfactory test animals. It deserves clinical trial as an anthelmintic, using the same routine as for thymol. Its dosage for administration must be worked out cautiously. H. E. R.

Sollmann, T. Observations on paradichlorbenzene and paradibrombenzene. *J. Pharmacol. and Exper. Therap.*, 1919, **14**, 243.

Paradibrombenzene has a less disagreeable odour and taste than paradichlorbenzene. Both are highly toxic for earthworms. They deserve clinical trial as anthelmintics when their toxicity has been accurately determined. H. E. R.

Abel, J. J., and **Macht, D. I. Histamin and pituitary extract.** *J. Pharmacol. and Exper. Therap.*, 1919. **14**, 279.

Histamin, if sufficiently dilute, produces the same effect as pituitary extract on the uterus of the mouse, causing contraction, whilst concentrated pituitary extract acts like the stronger solution of histamin, producing relaxation. This correspondence in effect does not necessarily mean identity in composition. The uterus of the rat, however, behaves differently to the two, and the cause of this difference is being investigated.

The hypothesis that histamin exists in the posterior lobe of the pituitary as a compound and as free histamin in equilibrium with the compound, is being tested. H. E. R.

Hjort, A. M., and **Eagan, J. T.** *J. Pharmacol. and Exper. Therap.*, 1919, **14**, 211.

Benzylcarbinol or β-phenylethylol, also known as rose oil or orange oil, has about the same toxicity as benzyl alcohol, but is more stable and has superior properties as a local anaesthetic. H. E. R.

Langenstrass, K. Untersuchungen über spezifische Niederschläge mittels des Interferometers. [**Investigations of specific precipitates by means of the interferometer.**] *Fermentforsch.*, 1919, **3**, 1.

The author has attempted to ascertain the relations between precipitin and antigen by means of the interferometer. This instrument is able to detect very fine differences in the composition of albuminous fluids. Various proportions of immune sera were added to normal sera and the interferometer readings taken in different dilutions. In this way one should be able to ascertain whether the process of precipitation were a purely physical (colloidal) phenomenon, or whether the reaction in part obeyed the laws of chemical union. According to L. the antigen is passive in character. The precipitin is a 'protective ferment'. The products of its activity are degradation compounds which change to a certain extent the hydrogen-ion concentration of the substrate and produce flocculation. Hence the precipitin is the 'key', and its action is a chemical one. Later, or possibly at the same time, a colloidal effect takes place, which is evidenced by obvious flocculation. C. G. L. W.

RADIOLOGY AND ELECTROLOGY

Radio-diagnosis

Roubier. Quelques considérations sur la comparaison des examens cliniques, radiologiques et bactériologiques des crachats chez les militaires suspects de tuberculose. [**Comparison between clinical, radiological, and bacteriological examinations of the sputum of military patients suspected of tuberculosis.**] *Progrés méd.*, 1919, June. (*J. de radiol. et d'électrol.*, 1919, **3**, 471.)

In this article the author compares the clinical, radioscopic, and bacteriological results of examination of 1,000 cases of suspected tuberculosis. He insists especially on the interest of the radiological examination which is absolutely indispensable, and reveals lesions which have remained unsuspected, and shows the extent of those already determined by clinical examination. But it is the examination of the sputum which proves the tuberculous nature of the observed lesions.

(1) Cases in which *B. tuberculosis* was found (151 per 1,000, of which 141 were tuberculosis of the apex).

(*a*) In 90 per cent. of these cases there was concordance of the clinical and radiological results of examination without always absolute parallelism. The signs shown by the screen were modifications of the image, which varied from simple homogeneous diminution of transparency with defective illumination on coughing, up to complete opacity with clean or indefinite limits; often there was observed a dappled or marbled appearance, a spotted aspect, or outlines of cavities. Generally on the screen the lesions appeared of greater extent and more advanced than was the case on auscultation.

(*b*) In 8·5 per cent. of the cases there was discordance between the clinical examination and the radiograph: in certain cases there was radiological evidence without clinical signs; in others, clinical signs without appreciable modification of the radioscopic image. (The author himself points out that the number of these cases would have notably diminished if the radioscopic examination had been completed by an instantaneous radiograph.) These were cases of very early localized lesions.

(*c*) Some rare cases of bacilli in the sputum without definite clinical or radioscopic signs. In most cases of tuberculosis of the middle or base of the lung the screen confirmed the topographical diagnosis by some modifications of transparency, and by a reaction at the hilum on the affected side.

(2) Patients suspected of tuberculosis with negative bacteriological examinations (304 per 1,000).

(*a*) In most of these cases where there was association of the radioscopic and clinical signs there was either frank evolution of tuberculosis with symptoms of softening, in which all the radioscopic signs previously noted could be observed, or chronic tuberculosis with a tendency to induration, or pleuro-pulmonary sceleroses, relics of former tuberculosis which had healed up. The screen also showed a homogeneous diminution of transparency at the apices, with or without a pointed appearance of the apices from transverse retractions of the upper part of the chest (former tuberculosis healed). Sometimes calcified nodules were found, or dark lines from the hilum and, very rarely, a cavity.

(*b*) Cases where clinical symptoms at the apices existed without radiological modifications (a matter either of simple apical bronchitis, of pleurisy, or of apical cortico-pleurisy).

(*c*) Cases with radiological changes in the apices without clinical signs: calcified nodules (healed lesions), obscuration or opacity of the apices. (The author supposes that these modifications were the result of slight parenchymatous fibrosis, or of adhesive pleurisy at this level.) In the case of those suspects with negative bacteriological examinations, the symptoms were consonant with an adhesive basal cortico-pleurisy (dark shadows running from the hilum to the diaphragm with irregularity of the dome, and partial or complete disappearance of the sinus), or were due to the results of former sero-fibrinous pleurisy.

(3) 543 of the 1,000 patients examined were ‘pseudo-tuberculous’, with or without pleuro-pulmonary lesions, and not yielding tubercle bacilli.

S. U. L-B.

Honeij, J. A. Influenza et broncho-pneumonie. Étude de l'épidémie au point de vue radiologique. [**Influenza and broncho-pneumonia. Radiological point of view of the epidemic.**] *Am. J. Roentgenol.*, 1919, **6**, 226. (*J. de radiol. et d'électrol.*, 1919, **3**, 471.)

A clinical and anatomo-pathological study of 91 cases of influenza, completed by an important radiological study. All these cases were minutely followed from their beginning to their end, by cure or death, by means of a movable apparatus which enabled the patients to be examined in bed.

The following are the radiological characteristics of influenza:—The pulmonary tissue appears as if veiled by a cloud, and this causes a diminished contrast between it and the bronchi. This obscuration is more marked in the internal part of the lung and extends from the apex to the base, rendering the mediastinal and cardiac contours less distinct. The costo-diaphragmatic sinuses are more or less effaced and the diaphragm is often raised. The bronchi appear larger, their shadow is wider and denser, and they can be traced particularly to the right base. In some cases the right auricle is enlarged. When recovery is taking place the pulmonary obscurity is the first to disappear, the opacity at the hilum is the last. In some cases the diagnosis of influenza was given solely from those radiological appearances, and before the appearance of any clinical signs; time confirmed the diagnosis.

When the complaint is becoming broncho-pneumonic the opacity of the bronchi is accentuated and enlarged, then from 6 to 8 cm. of the hilum dark zones appear, tending to become confluent, and take on the appearance of a smoke ring.

In some cases resolution can begin at this stage, but in the majority of cases the inflammatory process continues, giving the appearance of pseudo-lobar pneumonia: sometimes the whole lung is thus affected, and one can then see on the other side the same stages succeed one another. Dilatation of the right auricle and pulmonary artery early accompanies broncho-pneumonia; sometimes there is also a certain amount of aortic dilatation. The convexity of the diaphragm on the affected side is accentuated; it may be seen to rise from two to three intercostal spaces. S. U. L-B.

LANCE. Étude expérimentelle des manœuvres de Forbes et d'Abbott dans le traitement des scolioses graves. [**Radiology of severe scoliosis.**] *Rev. d'orthop.*, 1914, 3e sér., **5**, 405. (*J. de radiol. et d'électrol.*, 1918, **3**, 139.)

We deduce from this article the following indications relative to the radiological study of vertebral rotation.

1. Spinous processes. If no rotation exists, the spinous process is vertical and the shadow of its point is situated on the vertical axis of the vertebra. If there is rotation, the shadow of the point of the spinous process is projected to the right or left of this axis. It is directed in an inverse direction to the rotation of the vertebral body. The utilization of a small opaque orientation mark placed on all the processes enables that one which has been displaced to be distinguished with ease.

2. Lateral arches. Their projection is made on each side of the vertebra in the form of a little clear, oval, vertical zone, surrounded by a dark line. The whole forms two superposed rows on the vertebral column. If there is no rotation, the distance between each of these zones and the corresponding edge of the vertebra is the same on both sides. If there is rotation, it is unequal and more of the vertebral column appears on the side towards which the latter has turned.

3. Transverse processes. Their projection is equal on both sides; they appear foreshortened owing to their being oblique, from in front, backwards, and from within, outwards. When the vertebra turns, the transverse process, which is in front, is seen more and more transversely and seems to lengthen, that which is behind appears diminished and its shadow ends by disappearing into that of the vertebral column.

4. Ribs. If there is no rotation, the head of ribs is not visible in its entirety on each side of the vertebral column, the shadow of which partly hides the costo-vertebral articulation. If there is rotation, the costal head becomes more or less visible on the side which is in front. It is even possible to observe the articular spaces. On the opposite side, a more or less considerable portion of the head and of the neck are eclipsed by the shadow of the vertebral column. W. S. L-B.

OHLMER. Atrophie osseuse. [**Bony atrophy.**] *Rev. d'orthop.*, 1918, April. (*J. de radiol. et d'électrol.*, 1918, **3**, 138.)

Under the title of bony atrophy of Sudeck the author studies the well-known atrophy that attacks a bone in certain pathological conditions in the vicinity of a tubercular focus, an articular lesion, or a fracture. This work is based on a radiological examination of six cases of fracture caused by injuries in the war.

At the beginning the transparency of the bone (under the rays) during the acute period, is not uniform, but spotted with points that have remained denser. The spongy tissue is pierced with holes more or less circumscribed by some not very marked partitions that are thickened.

When fully established the shadow is no longer light and soft, but clear, the structure of the bone showing plainly, but the transparency is great and in a uniformly clear background very fine quadrilaterals of bony partitions are depicted. In the spongy tissue the entire absence of structure is very noticeable. The limits of the bone are marked by a very sharp but fine line. In bad cases the transparency can spread over the whole bone, which looks as if composed of glass. The author attributes this state to trophic lesions of nervous origin. In fractures consolidation is retarded; when this atrophy exists, one might even mistake them for cases of pseudoarthrosis.

W. S. L-B.

Lécène et **Gauducheau.** Réactions électriques des muscles et des nerfs chez des blessés cliniquement guéris du tétanos. [**Electrical reactions of the muscles and nerves in the wounded cured surgically of tetanus.**] *Compt. rend. Soc. de biol.*, 1918, 22 Juin. 657. (*J. de radiol. et d'électrol.*, 1918, **3**, 143.)

This article deals with two patients: one had been discharged from the hospital two months previously, the other had not had a paroxysm for twelve days. In a general way a galvanic and faradic hyperexcitability is verified, which persists, becoming weaker in the course of weeks.

Nerves. In certain cases, and only on the nerve-trunks that have been most affected by the paroxysms, galvanic clonus can be obtained: after the circuit is closed, the current being kept constant, the muscles innervated by the excited nerve are moved by a series of contractions that tend in general to complete tetanus. This ceases at the opening of the circuit.

Muscles. A sufficiently weak excitation at the motor point determines a state of clonus persisting during the whole passage. Rapid, full, regular shocks do not lead to tetanization, if the voltage has been well chosen (undulatory reaction). With a higher voltage one notices, after one or sometimes two brief and rapid shocks that follow the closing of the circuit, a tonic contraction that persists till the opening of the circuit.

With a still more intense current, or if one makes the examination a few days after the disappearance of the paroxysms, there is a concomitant stiffening of the neighbouring muscles and sometimes several limbs. The position is then the same as that taken up during the tetanic crisis. According to the length of time that passes from the acute period the weaker these phenomena become. But three months after the cure a tonic contraction can still be obtained by excitation of the nerve.

W. S. L-B.

Radio-biology.

Pais, A. Excitation des organes hématopoïétiques dans le paludisme. [**Radio-excitation of the haemopoietic organs in malaria.**] *Arch. d'électric. méd.*, 1919, **27**, 257.

The author points out that though it has long been known that X-rays can excite the activity of vegetable cells, in animal tissues such phenomena are so rare and uncertain that they have been regarded as inflammatory or even as pathological. He maintains, however, that under suitable conditions stimulation is constant and normal. As evidence he adduces the changes occurring after irradiation in haemopoietic and lymphatic tissues, viz. (1) the polynucleosis which follows all irradiation and precedes the phenomena of lymphatic destruction: (2) phagocytosis in the spleen, in the bone-marrow, and in the vessels, and (3) the hyperactivity of the medulla at the expense of the fatty tissues, and the increased numbers of eosinophils, mast cells, and erythroblasts. These phenomena appear after suitable irradiation, not only of the whole animal, but also when irradiation has been confined to the spleen. Upon the view that this cellular proliferation might bring about a transitory exaltation of the power of resistance and of defence of the organism against infectious disease, he investigated paludism (a disease in which a reaction of the haemopoietic organs, the white cells of the blood, and the endothelial cells, accompanies the progress of the infection) and expected to find that irradiation is accompanied by modification in the cycle of infection. This evidence he sought in the behaviour of the patient's temperature. Radio-therapy in malaria has already been tried on many occasions, but the conditions of the irradiation and the results of the treatment have been very variable. In all instances, however. the treatment has been based on an attempt to obtain destruction of the pathological elements or of the haematozoa. P. worked on other lines. He sought to stimulate the natural defensive mechanisms by employment of excessively small doses of extremely hard rays. Filtration was through 2–4 mm. of aluminium and the distance from the X-ray bulb was regulated so as to irradiate uniformly the whole substance of the spleen. From a series of 3,000 observations he believes that irradiation of the spleen of malarial patients can profoundly modify the temperature curve in various directions. Speaking generally, administration of large doses (by which he signifies doses such as those generally employed in treatment of these cases) aggravates the condition: on the other hand small doses and 'infinitely small doses' tend to diminish the intensity of the attacks, retard their onset, or even suppress them entirely. The actual dose requisite to bring about these results varies in the different varieties of ague. The period in the malarial cycle at which the irradiation is administered is of prime importance. Though no details can be given with precision, it appears that the closer the irradiation to the time of onset of the attack the greater its effect. In the case of benign tertian ague the optimum time for irradiation is 3–4 hours before the attack.

The author then discusses the explanation of these phenomena. He considers that the sensitiveness of any particular type of cell to irradiation is related to its condition of functional activity at the time of irradiation. Thus, if a stimulating dose be given at a time when the defensive mechanism is at the height of its activity, the result on the patient will be beneficial; if the dose of irradiation be 'destructive' towards the defensive mechanism, and particularly if it be given at a time when this defensive mechanism is at the height of its functional activity, the result to the patient will be injurious.

Not only in respect of the actual disease which was placed under investigation is the paper of importance (particularly at the present time when so many cases of chronic malaria have resulted from the war) but also it is important in respect of the radio-biological conceptions underlying the work. So far as concerns the question of radiological treatment of malaria two points of view are possible (*a*) the direct destruction of the protozoa by the rays and (*b*) their indirect destruction by way of the normal defensive mechanisms. To judge from recorded observations the first method has not succeeded, though there can be no doubt that the malarial parasite—like other lowly animal organisms—must be vulnerable by the rays. On the other hand, the doses of X and radium rays which lowly organisms can support without apparent modification is enormous, so that it might well be that any attempts in this direction would be provocative of very serious damage to the normal tissues of the patient. The value of Pais's paper lies in the fact that he indicates the possible (indeed, he asserts the actual) advantage of building up the natural defensive mechanism by means of stimulatory small doses of rays. Fraenkel[1] has advanced a similar view in respect of tuberculosis.

So far as the radio-biological conceptions underlying the paper are concerned one cannot value it so highly. The physiology of the haematopoietic and lymphatic systems is so complex that one can hardly assert, for example, that a haemal leucocytosis is evidence of an increased formation of leucocytes (stimulation or hyperactivity); it might equally well depend upon an altered distribution of leucocytes in the system. This is one of the difficulties attending the use of extremely small doses. Where the dose is enormous and destruction takes place as evidenced by leucopenia, diminution in size of the spleen and lymphatic glands throughout the body, and perhaps by the actual presence of lymphocytic and leucocytic débris, the scientific certainty is great and demonstrable. The author's knowledge of literature bearing upon the stimulative side of ray action appears to be limited, and even on the destructive side he should have sought to correlate his view that the sensitiveness of cells to irradiation depends upon their state of functional activity at the time of irradiation with Mottram's observations upon the effects of radium rays upon the nucleus. Mottram[2] showed that the nucleus in mitosis is at least seven times as vulnerable as during the resting stage. It may be that increased sensitiveness is manifested under both conditions, reproductive and functional, but so far there is no evidence of this. Indeed, the evidence of a direct action of rays upon the chromatin of the nucleus is so considerable, while evidence of their action upon the cytoplasm (and it is mainly upon the cytoplasm that functional activity depends) is so scanty, that one is compelled to ask for further proof of the author's contention in respect of the ultrasensitiveness of cells to irradiation during functional activity. W. S. L-B.

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[1] Cf. *Med. Sci.*, 1919, 1, 125.

[2] Arch, *Middlesex Hosp. Twelfth Cancer Rep.*, 1913, 98.

Radio-therapy.

Pollitzer. Über asthmaartige Symptome als Röntgenwirkung bei Leuchamien und als Vaccinewirkung bei Abdominaltyphen und die Pathogenese dieser Erscheinungen. [**Asthmatic symptoms caused by the action of X-rays in leukaemia and by the action of vaccine in typhoid fever and the pathogenesis of these phenomena.**] *Med. Klin.*, 1919, **19**, 457. (*Zentralbl. f. Chir.*, 1919, **46**, 821.)

The author observes that, in irradiation of leukaemia, there is sometimes a rapidly appearing bronchitis with eosinophilia and relative pulmonary congestion. The condition rapidly disappears and is associated with irradiation of the spleen. A very similar condition is sometimes met with after antityphoid vaccination. Both syndromes appear to be connected and to be pathological results of inoculation with foreign albumin, in the one case bacteria, in the other the degenerated leucocytes. The leukaemia syndrome appears to be connected with bronchial asthma. S. U. L-B.

Electro-diagnosis.

Gauducheau, R. Des réactions électriques au décours du tétanos. [**Electrical reactions during the decline of tetanus.**] *J. de radiol. et d'électrol.*, 1919, **3**, 403–7.

The detailed account of the electrical reactions of the muscles and nerves in two cases of acute localized tetanus, one case being examined when technically cured, the other when nearly so, shows how signs of latent trouble were disclosed in muscles apparently cured, and also in muscles which had appeared to escape the disease.

In one case tonic contractions were produced four months after the cessation of the tetanic crises.

The signs found were:—Lowered 'threshold' value for the stimulation at 'break'. Two stages of altered form of contraction, the first with increased maximal height but irregular and easily exhausted, the second of small amplitude but regular; galvanotonus; galvanic clonus; contro-lateral reflex contraction of the erectores pilorum.

These signs form a syndrome which is not only found in tetanus, but has also been seen in malaria cases at Salonika and in technically cured 'shell-shock' patients. Some of these characteristics of hyperexcitability have been described in tetany.

Another observation was a contraction *en masse* of the affected muscles when stimulation was applied on the same limb but at a distance, or on the opposite limb. The latent period and other features of this lead the author to class the contraction as a reflex similar to that described by Bourguignon in central nervous lesions. N. H. M. B.

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REVIEWS

INFLUENZA

Epidemiology. In the report showing the official returns of influenza in Switzerland from July 1, 1918, to June 29, 1919, it is stated that a large number of cases never sought medical advice, either because the attack was so mild or because there was no doctor in the neighbourhood. Moreover, the extra amount of work due to the epidemic often prevented practitioners from notifying the disease. Lastly, numerous cases of influenza were not recognized as such, and helped to swell the statistics of other diseases, though by way of compensation many examples of other diseases were wrongly attributed to influenza. Taking all these circumstances into consideration, it is probable that the total number of cases was three times that actually notified, or about 2½ millions, of which 2 millions in round numbers occurred in 1918. The incidence of the disease or relation of the cases to the population was about 58 per cent. for the whole epidemic, and 50 per cent. for the year 1918 only. The case mortality was 1·1 per cent. On the supposition that the morbidity ran more or less parallel with the mortality, 30 per cent. of the cases occurred under 15 years of age, 65 per cent. between 15 and 49, and only 5 per cent. in persons of 50 and over. Under these conditions the incidence of influenza would be 50 per cent. for the age group below 15, 70 per cent. for the age group 15 to 49, and 20 per cent. for the ages above 50. Generally speaking, the epidemic reached its culminating-point in eastern Switzerland one or two weeks later than in western Switzerland, which indicates that the epidemic passed from west to east, and consequently invaded the country from the west. It was obvious that the number of cases notified did not represent the exact degree of the diffusion of the epidemic. In regions which were out of the way, thinly populated, and not provided with doctors, fewer cases were notified than in others, though it could not be inferred that the incidence was less than in other districts. The male sex showed a much higher mortality than the female, this being partly due to the remarkably severe character of the epidemic in the Swiss army (vide *Medical Supplement*, 1918, **1**, 445 *a*). In the male sex about three-quarters of the deaths occurred among the classes aged 20–50; in the female sex this proportion was about two-thirds. The rest of the deaths were about equally distributed among both sexes, three-fifths occurring in the age groups above 20, and two-fifths above 50. The mortality of the age group 20–50, doubtless as the result of mobilization, was 1½ times higher in the male (6·5 deaths per 1,000) than in the female sex (4·4 deaths per 1,000). In the age group below 15 the mortality was much lower and the proportion reversed (2 deaths per 1,000 for females and 1·6 deaths per 1,000 for males).

In his report on the mortality from influenza in Scotland during the epidemic of 1918–19 Dunlop arrives at the following conclusions: (1) The mortality was much greater than in any previous epidemic since 1855, being more than six times as large as that of the epidemic of 1900, which was the previous greatest. (2) The mortality from the recent epidemic greatly exceeded that of other infectious diseases. In the next most fatal epidemic, that of scarlet fever in 1874–5, the mortality was only about one-quarter of the recent influenza mortality. The maximum mortalities from epidemics of measles, typhus, and whooping-cough, amounted respectively to 3,639, 3,272, and 3,212, which figures are small in comparison with the 17,575 deaths caused by the recent epidemic. In 1917 phthisis was the ascribed cause of death in 5,073 cases, which number is less than one-third of that caused by influenza. (3) A large proportion of the fatal cases occurred among young adults, fully 50 per cent. of the deaths being between the ages of 15 and 44, and 23 per cent. between 25 and 34. (4) Deaths of which influenza was one of two or more named causes greatly outnumbered those of which influenza was the sole named cause, the former numbering 14,699 and the latter 2,876. (5) By far the most frequent association of death was pneumonia, deaths from influenza and pneumonia in association numbering 11,236 out of the total of 17,575.

Wiese is of opinion that an obscure febrile disease observed by Schittenhelm and Schlecht on the Eastern front in the autumn of 1917 (vide *Medical Supplement*, 1918, **1**, 135 *a*) and a similar epidemic observed by himself in the southern part of the Eastern front from October 1916 to January 1917 were really influenzal in character. He dismisses the hypothesis of pappataci fever, as the cases occurred during the cold season, and pappataci fever and the phlebotomus fly were not met with in that region.

In their account of the epidemic in Portland prison and its official quarters in October and November 1918, Smith and Saunders state that there were 492 cases, only 8 of which occurred among the 270 convicts in the prison, and the rest among the officers and their families. An exceedingly large proportion of the whole community was attacked, viz., 40·4 per cent. 65·3 per cent. of all the school children in the community were affected. Although the mortality among the general population of the island was distinctly high, especially among young adults, no deaths occurred in the prison or its official quarters, a result attributed by the writers, first to the excellent housing conditions and entire absence of overcrowding, and secondly to the ability of the patients, mothers of families excepted, to take to their beds at the first sign of illness and remain there till convalescent.

In their account of the epidemic of influenza among American troops in England, Meader, Means, and Hopkins state that the mortality was about twice as high on board transports as on shore, viz., 4 per thousand per month at sea and 2 per thousand per month on shore. The high mortality at sea was probably due to debilitating circumstances, such as unpalatable and insufficient food, poor ventilation, overcrowding, and exposure to cold and wet, and probably still more so to the virulence of the infecting organisms. The troops were all newly recruited and came from cantonments where a highly virulent organism was prevalent.

Ehrenberg finds the most satisfactory explanation of various, apparently anomalous, phenomena associated with the spread of influenza in hospitals to be (1) that the disease is not infectious during the first day of the patient's symptoms and (2) that infection is almost invariably by direct contact, not by utensils or the agency of a third party. The facts on which he bases these hypotheses are as follows: At his hospital in Falun, during the epidemic of influenza in the autumn of 1918, there were 17 wards, large and small, and 76 beds, to which 20 other beds were added for part of the time. Between August 2 and December 15 there were 143 cases of influenza admitted, of which 39 were uncomplicated. Every case of influenza admitted was strictly isolated, whatever the stage of the disease. The staff of the hospital numbered 25. All attended both influenza cases and others; the only precautions taken to prevent infection of non-influenzal cases was the rule that attendants washed their hands between nursing influenzal and other cases; the eating and drinking utensils of the two classes of patients were kept separate. Of the staff, five had contracted influenza shortly before this epidemic broke out. All the remainder, with only two exceptions, developed influenza, and were warded within a day of the onset of symptoms. The non-influenzal cases treated in the hospital during the same period numbered 259. Among them there were only three cases of transient fever suggestive of influenza. Two of these cases were at once isolated; but even in these cases influenza was probably not the cause of the slight rise of temperature. Ehrenberg concludes that these striking differences in the morbidity of staff and patients cannot be accidental, but must be the expression of fundamental factors governing the propagation of the disease.

Zander finds that the school plays little part in the propagation of influenza, and that the following data afford evidence in favour of Ehrenberg's hypothesis that influenza is not infectious during the first day of the disease. In a school attended by 711 scholars between the ages 7 and 14, there were 24 classes. Special arrangements were made during the influenza epidemic in the autumn of 1918 to ascertain the causes of absences from school with a view to finding out the incidence of influenza among the scholars. Altogether there were 419 cases of influenza. Zander drew curves showing the incidence of the disease (*a*) in the school, (*b*) in the immediate neighbourhood of the school, and (*c*) in the whole of Stockholm. The three curves thus obtained were almost identical. Zander takes this parallel course as evidence of the school's innocence of propagating the disease. But in three of the 24 classes there was an explosive outbreak of influenza following a curve not conforming to the general curve elsewhere in Stockholm at the same time. Apart from these exceptions (which Zander assumes arose as a result of infection by patients with too slight a form of influenza to keep them at home as early as the first or second day of the disease) it would appear from this investigation that schools ought not to be shut in times of influenza epidemic, always provided the rule is made of scholars being kept at home, or sent home from school, as soon as symptoms of influenza manifest themselves.

Symptomatology. In ordinary uncomplicated influenza the fever lasts only a few days or a week, and only rarely persists more than one or two weeks. Consequently cases with protracted fever in which the disease has not affected other organs than the lungs are of considerable interest. In the last epidemic, out of a total of about 300 cases of influenza, Wolpe saw examples of protracted fever in 24 cases, or 8 per cent. The duration of the fever in these cases varied between 14 days and 7 months: in 13 it was between 2 and 4 weeks, and in 11 between 1 and 7 months. The temperature was of the high continued type or more frequently of a remittent character, and in some cases showed intermissions of several days. In all the cases there were definite changes in the respiratory organs, such as bronchitis, pneumonia, pleurisy, empyema, and mixed forms of these diseases. The disease ran a severe course in all, although in the cases of bronchitis the objective signs were often relatively slight. None of the cases of uncomplicated influenza or bronchitis died, whereas 5 out of 8 cases with suppurative processes were fatal.

During the last epidemic Lichtwitz of Altona found the **capillary pulse** present in 33 per cent. of the cases complicated by pneumonia, and in 20 per cent. without any obvious pulmonary focus. It was associated with a pulse-rate ranging from 70 to 140 and very often with a low blood-pressure. A rapid and soft pulse was usually though not invariably present. It was noteworthy that the capillary pulse was found with temperatures ranging from 98·6 to 105·8 and not infrequently lasted longer than the fever. It was equally remarkable that it was present not only when the skin showed a febrile redness, but also in patients with pale skin, cyanotic pallor, and all the signs of vasomotor paralysis. It was even found in cases of cardiac failure with a very small frequent pulse, feeble heart sounds, and pronounced cyanosis shortly before death. The frequency of the capillary pulse in so large a proportion of cases of influenza accords with the other changes seen in the peripheral vessels, such as the patchy redness or cyanosis of the face without cardio-pulmonary changes, the tendency to haemorrhage from the mucous and serous membranes, and the relative frequency of phlebitis and arteritis. The chief interest of these observations is that the capillary pulse in influenza does not depend on the body temperature, the redness of the skin, or the action of the heart, but is a manifestation of a toxic lesion of the arterioles and capillaries.

Deusch has recently seen a number of cases of **post-influenzal dyspepsia** at the Rostock University Polytechnic. None of the patients had suffered from gastric disturbance prior to their attack of influenza. In most cases the symptoms lasted for several months. He attributes the condition to a hyperaesthesia of the gastric mucosa due to affection of the sensory nerve endings in the stomach by the influenza toxin. Disturbance of the motor functions of the stomach was relatively rare, but most of the cases showed some disorder of gastric secretion. Sub- or anacidity was the rule, being due to a toxic involvement of the vagus.

The **genito-urinary complications** of influenza are discussed by Bugbee, who, after alluding to the recent papers by Sofré (vide *Medical Supplement*, 1918, **1**, 385 *b*), Dalimier (*ibid.*, 1919, **2**, 74 *b*), Dunner and Papko (*ibid.*, 166 *a*), and Lichtenstern (*ibid.*, 166 *b*), reports 39 personal cases. In 22 there was infection of one or both kidneys, in 5 perinephritic abscess, in 4 prostatic abscess, in 6 epididymitis, and in 1 seminal vesiculitis. Of the 22 renal cases 14 gave a history of no previous urinary symptoms.

In autopsies on 360 cases of influenza, 270 of which occurred among civilians and 90 among soldiers, Fahr met with only 4 cases of glomerular nephritis, 3 of which were found among soldiers who had been on active service. He points out that certain factors inherent in life at the front, such as exposure to cold, increase the liability to glomerular nephritis, so that this form of renal disease was relatively frequent among soldiers. The renal lesions seen in the civilian cases showed no uniformity, as was to be expected from such a mixed infection as influenza.

Nervous system. Re, who is an assistant at the Institute of Medical

Pathology of Pavia University, is convinced that lethargic encephalitis, which has been attributed to botulism or Heine Medin's disease or regarded as an independent disorder, is merely a rare nervous complication or rather manifestation of influenza. He recalls the fact that during the pandemic of influenza in 1890–1 cases were described by Bozzolo in Italy, and by Ebstein in Germany, of a lethargic affection resembling the present one, and was regarded by them as a cerebral complication of influenza. Similarly all the 13 cases observed by Re occurred in districts where influenza was prevalent, and in patients in whom the lethargic symptoms were preceded or accompanied by other symptoms and signs of influenza.

The influenzal origin of lethargic encephalitis also appears to be held by Heiman, who reports 8 cases of post-influenzal encephalitis from the Pediatric Service of Mount Siniai Hospital, New York, in children aged from 4 months to 13½ years. He distinguishes three main forms of encephalitis following influenza according to their severity and most prominent symptoms, viz., (1) the irritable, (2) lethargic, and (3) lethargic with paralysis. Only one of the cases showed definite changes in the cerebrospinal fluid, viz. lymphocytosis. In two cases the children became imbeciles, and in three others the paralysis, though considerably improved, did not disappear.

On the other hand, Grosz and Pappenheim agree with Economo in regarding lethargic encephalitis as distinct from the encephalitis seen in influenza. A study of the literature and their own experience show that in spite of the frequent occurrence of severe cerebral symptoms in influenza, especially meningeal manifestations, gross lesions of the nature of haemorrhagic encephalitis are rare, and that in a certain number of the cases the haemorrhages are not to be regarded as true inflammatory foci. In concordance with this is the fact that in the cerebrospinal fluid, apart from a rise of tension which is not always present, there is no evidence of meningitis in influenza. These circumstances favour the view that the cause of the cerebral symptoms in influenza in the great majority of cases is not an infective involvement of the brain, but probably an intoxication of the brain and its vascular system. On the other hand, inflammatory changes in the cerebrospinal fluid are frequent in lethargic encephalitis.

The meningeal complications of influenza are classified by Schreiber into (1) meningitis, (2) meningeal reaction, and (3) meningism. Purulent meningitis does not occur in influenza and even serous meningitis is uncommon. The meningeal symptoms as a rule are accompanied by little or no change in the cerebrospinal fluid. Schreiber reserves the term 'meningeal reaction' for a condition intermediate between serous meningitis and meningism and characterized by definite clinical symptoms and a slight cellular reaction. He records two examples in which the spinal fluid was under transient hypertension, but did not contain an excess of albumin, and showed only a very slight lymphocytosis. Meningism in which the cerebrospinal fluid remains completely normal was the most frequent meningeal complication observed in the last epidemic. Lumbar puncture not only settles the nature of the meningeal complication, but has also a valuable therapeutic action in diminishing the intense headache from which the patients suffer.

According to Stangl nearly 1 per cent. of 3,400 cases of influenza at the Cook County Hospital had symptoms suggestive of meningitis or cerebral involvement. They varied from slight neck rigidity and unilateral or bilateral Kernig's sign to deep delirium and marked rigidity of the neck, and in one case to opisthotonos. The cases were divided into two groups, the first consisting of eight cases, in which a diagnosis other than influenza, such as epidemic meningitis, uraemia, tuberculous meningitis, or apoplexy, was incorrectly made, as was shown at the autopsy.

The spinal fluid in these cases was constantly under increased tension, but the presence of globulin, albumin, and increase of cells was variable; the fluid was always sterile. The second group consisted of 21 cases diagnosed as influenza or influenzal pneumonia with meningism, the latter diagnosis being made after negative spinal fluid examination. The tension of the spinal fluid in these cases was increased, but the fluid was always clear. The albumin and the globulin tests were positive in one instance, but in no case was there an increase in the lymphocyte count.

Merklen reports two cases of acute ascending paralysis which occurred during an epidemic of influenza in Brittany without positively asserting that they were of influenzal origin. The arguments in favour of such a view were that in one case the symptoms of the onset closely resembled influenza, and that the other patient came from an epidemic focus and was suffering from a dental abscess which may possibly have been due to influenza.

Tanfani, of the Neurological Centre at Tarentum, states that during the last epidemic of influenza the nervous complications chiefly affected the upper limb, probably in topographical metameric relationship with the pulmonary affection. He records four cases of influenza complicated by broncho-pneumonia, two of which developed unilateral musculospiral paralysis, one bilateral circumflex paralysis, and one left hemiplegia, which he attributes to cerebral haemorrhage like the cases recently reported by Marcovici (vide *Medical Supplement*, 1919, **2**, 167 *a*).

At a meeting of the Hamburg Medical Club on May 27, 1919, Nonne reported 11 cases of nervous sequelae of influenza. Apart from sensory changes in the trigeminus area none showed any sensory symptoms. In all cases the cerebrospinal fluid and tendon and cutaneous reflexes were normal. The symptoms occurred either directly after the attack of influenza or some weeks later. All possible combinations of paralysis of the cranial nerves were seen. The facial nerve, the eye muscles, and the nerves to the pupils were most frequently affected. Signs of bulbar disturbance were very frequent, whereas the optic nerve was only once affected and in a slight degree. The extremities were never really paralysed, but only involved in the general debility. Contractures with increase of muscular tonus and signs of motor irritation were frequent. Some patients showed the exact appearance of bulbar paralysis, others closely resembled cases of paralysis agitans sine agitatione, and others, again, cases of the recently described extra-pyramidal symptom-complex (vide *Medical Science*, 1919, **1**, 209). The prognosis as a rule was good, but two cases died with symptoms of bulbar paralysis or prostration and collapse. Well-marked symptoms of meningitis were present in only one case, in which, however, the cerebrospinal fluid was free from any signs of inflammation.

Meyerhof records six cases of abducens paralysis in influenza. In two cases which came to autopsy no macroscopical lesions were found in the nuclear region in the form of haemorrhages or other gross changes. The cases thus confirmed Bernheimer's view that the ocular palsies following influenza, like those following diphtheria, are caused by the action of the toxins on nerve tissue. There appears to be a specific toxin which in the case of diphtheria has a predilection for the nerves of accommodation, and in influenza for the sixth nerve. Both nerves and their nuclei are the most sensitive of the cranial nerves, as is shown in several diseases of the nervous system, especially syphilis.

At a meeting of the Berlin Laryngological Society on May 16, 1916, Kickhefel reported 4 cases of paralysis of the soft palate following influenza. Three of the patients were children aged 5–16, and one was an adult aged 33. None of the patients had had any symptoms of diphtheria, though no bacteriological examination appears to have been made at the time of the acute attack. In the subsequent discussion Bruck stated that he had shown a case of complete palatal palsy following influenza about 15–20 years ago. Peyser, on the other hand, emphasized the possibility of latent diphtheria in such cases, and Finder related a case of palatal palsy following a supposed attack of influenza in which throat cultures showed diphtheria bacilli.

Chodak also reports a case of palatal palsy in a child aged 6 years, accompanied by loss of the right knee-jerk following an attack which was said by the mother to be influenza, from which the rest of the family was suffering at the time. The condition lasted about two months. As in Kickhefel's cases, however, the patient was not seen during the acute attack and no bacteriological examination of the throat was made.

Guillain and Libert report a case of isolated paralysis of the serratus magnus following influenza in a soldier aged 31 which is of interest, (1) because influenzal neuritis has been relatively rare in the recent epidemic, (2) because only a few cases of isolated paralysis of the serratus magnus following infectious diseases have been recorded. The attack of influenza was severe being complicated by pneumonia, and the paralysis developed in convalescence.

Meissner found that intercostal neuralgia was a very frequent sequel of influenza, whereas trigeminus neuralgia was hardly ever seen. True intercostal neuritis also occurred with tender points in the course of one or more nerves, hyperaesthesia and hypaesthesia, and diminution or complete absence of the corresponding abdominal reflex. Occasionally there was a distinct paresis of the corresponding segment of the abdominal musculature.

In a paper on the causes of Quincke's oedema, Sieben records a case in a girl aged 13 in which a severe attack of influenza was followed in a month's time by chorea, at the height of which attacks of angioneurotic oedema occurred every 2 or 3 days. The left side of the face was always exclusively affected. There was never any fever, urticaria, or intestinal symptoms. As the chorea subsided, the oedema disappeared. Sieben is of opinion that both the chorea and the angioneurotic oedema were due to influenza, and suggests that many other cases of angioneurotic oedema which are not of intestinal origin are due to this cause.

According to Vorpahl **influenzal myositis** is a highly febrile disease occurring in or after influenza and characterized by a painful swelling of the muscles without changes in the skin. The prognosis is favourable, as all cases have hitherto recovered without leaving any residues in the affected muscles. The course is chronic and convalescence very slow. The affection is rare and appears to have been observed only in the influenzal epidemic of 1918. Myalgia, which is a constant phenomenon in influenza, is to be regarded as a mild form of influenzal myositis. In Vorpahl's case there was a very tender firm swelling of the nuchal muscles and tenderness without swelling in the extensors of both thighs and calf muscles accompanied by high fever and considerable leucocytosis. The disease ran a very chronic course but complete recovery took place. Whether the cause of the myositis is the *B. influenzae* or a mixed infection is not yet known. As regards treatment, salicylic preparations, quinine, baths, and hot air have little effect, but collargol was beneficial in Vorpahl's case. Other examples of influenzal myositis have been recorded by Burger (vide *Medical Supplement*, 1918, **1**, 340 *a*) and Hildebrandt.

Myalgia is described by Meissner as one of the sequels of influenza. One or more groups of muscles, especially of the back, showed a diffuse tenderness on pressure, without any localized tenderness at any of the nerve-pressure points. The patients declared that they had not had any trouble of this kind before their attack of influenza. The pain did not remain confined to one place, but first appeared in one spot and then in another, and was much worse in bad weather. Next to the back the nape of the neck was most often affected; in some cases the lumbar muscles were involved, but the extremities were very rarely attacked. There was never any fever.

Todd met with 16 cases of **thyroid involvement** in about 1,500 cases of influenza. In only six were the signs well marked. The remaining ten cases were slight and would probably have escaped notice if special attention had not been kept. With the exception of a girl aged 10, who developed hypothyroidism in convalescence and rapidly improved under thyroid treatment, all the cases showed varying degrees of hyperthyroidism. The time of onset of the thyroid symptoms and signs was very variable: in one it was noted on the sixth day of the illness, the other extreme was the twenty-first day. In all but one fatal case it developed during convalescence, and the onset was sudden in all cases.

According to J. C. and C. Regan **influenzal croup** is most frequent in children between the ages of 3 and 10, boys being more often affected than girls. The bacterial flora found is very similar to that noted in general among influenza cases. In the naso-pharynx there was a predominance of Pfeiffer's bacillus, pneumococcus and *Micrococcus catarrhalis*. In the cultures from the sputum streptococci, pneumococci, and Pfeiffer's bacillus were most common. In cultures from the larynx and trachea *post mortem* staphylococci were most constant, Pfeiffer's bacillus and pneumococci being next in order of frequency.

The symptoms of croup follow the attack of influenza after an interval of two to ten days and are similar to those of laryngeal diphtheria, the chief differences being as follows: In influenzal croup the tonsils and larynx are free of membrane, the mucous membrane of the throat having a deep-red, dry, glistening appearance unlike the more moist appearance common in diphtheria. The buccal mucosa is parched, and in the early stage the tongue is dry and feels hot to the touch. On auscultation numerous sibilant and sonorous rhonchi are heard. Lynah states that an occasional feature of influenzal croup is the absence of gradual progressive rhythmic inspiratory and expiratory dyspnoea which is frequent in diphtheritic croup. A persistent recurrent glottic spasm is sometimes met with which gives rise to a well-marked crowing sound, and if subglottic stenosis is present there is an expiratory croupy cough.

The following **surgical complications** of influenza are reported by Mitterstiller: (1) Bilateral mastitis in a woman aged 49. Although the mastitis developed during the attack, suppuration did not take place till several months afterwards, when an abscess in the right breast was opened, and *Staphylococcus pyogenes aureus* was found in the pus. (For other examples of this rare complication see *Medical Science*, 1919, **1**, 146, 253).

(2) Two cases of osteitis of the radius at the proximal and distal ends respectively. In one case *B. influenzae* was found, and in the other bacilli resembling it. (3) Two cases of thyroid fistulae following suppurative thyroiditis in subjects of goitre. In one case Gram-negative bacilli and streptococci were found, and in the other bacilli resembling *B. influenzae*.

Calderon, Professor of Obstetrics in the University of the Philippines, considers that influenza exercises an injurious influence on **pregnancy** independently of broncho-pneumonia and pneumonia. In 7 out of 36 cases of influenza admitted to the obstetrical department of the Philippine General Hospital pregnancy was interrupted, although it was not complicated by broncho-pneumonia or lobar pneumonia. As coughing and asphyxia were not prominent in some of the cases in which pregnancy was interrupted, Calderon considers that the influenza toxin acts directly on the uterus. In this series the broncho-pneumonia and lobar-pneumonia complicating the puerperium were fatal in 100 and 76·4 per cent. respectively. Influenza also had a deleterious effect upon the foetus. Among 27 pregnancies there was one case of hyperpyrexia in a new-born baby and seven deaths, which included intra-uterine deaths and deaths which took place several hours after birth.

Schmitz, assistant at the Frankfort University Medical Clinic, gives the following figures showing the unfavourable prognosis of influenza in pregnancy. Of 37 pregnant women who contracted the disease 17 died, a mortality of 45·9 per cent., as compared with a mortality of 12·5 per cent. among 866 non-pregnant women, and 23·5 per cent. among 357 men. By adding his figures to those of Ottow, Wollner, Karlbaum, Benthin, and Seitz (vide *Medical Science*, 1919, **1**, 149, 150, 158), a total of 139 cases of influenza in pregnancy was obtained with 61 deaths, a mortality of 43·9 per cent. Schmitz attributes the unfavourable course of influenza in pregnancy not only to changes in the respiratory mechanism and obstruction to the circulation, but also to a physiological swelling of the respiratory mucosa, so that there is a special tendency for pregnant women to develop broncho-pneumonia.

The frequency of **influenza in infants** is shown by the following statistics compiled by Ferreira of São Paulo, with regard to 115 infants living in close contact with cases of influenza, and as a rule in the same room. 19 were less than 6 months of age, 39 were between 6 months and 1 year, and 57 were more than 1 year old. In the first group 3, or 15 per cent., had influenza in a mild form, and this took place when all the members of the family, especially mothers and younger children, had contracted the disease. In the second group 23 or 38·9 per cent. were attacked. In the third group the infection was much more frequent as it occurred in 63 per cent. Generally speaking, therefore, it may be said that there is a real immunity below six months of age, which is only lost when the virulence of the germ is exalted by its multiplication in the adolescent and adult members of the family, especially the mothers who are liable to infect their infants both by contact and by their breast milk.

In a paper on the **influence of influenza on pre-éxistent diseases** Meissner of the Breslau University Medical Clinique distinguishes three groups of cases according as the pre-existent disease was aggravated, unaffected, or improved by the supervention of influenza. The first group comprised cases of acute nephritis and malaria, the second cases of pulmonary tuberculosis, aortic insufficiency and chronic interstitial nephritis, and the third nervous affections, such as hysteria or asthma.

Resemblance to typhus and gas poisoning. Coglievina was struck by the resemblance which severe cases of influenza presented to typhus on the one hand and to gas poisoning on the other. The resemblance to typhus consisted in a more or less intense conjunctivitis and catarrh of the respiratory system, the occurrence of epistaxis and haemoptysis and the frequency of nervous symptoms. In 15 per cent. of his influenza cases he observed fibrillary twitchings of the muscles of the face and other regions. Ataxia was observed in 35 per cent. 2 per cent. showed definitely katatonic symptoms which lasted a few days. 30 per cent presented violent states of excitement or confusion. Another resemblance to typhus was the occurrence of a morbilliform eruption. The resemblance to gas poisoning was shown by the penetration of the inflammation to the finest ramifications of the bronchi, giving rise to air hunger and cyanosis with death from asphyxia.

Morbid anatomy. Influenzal broncho-pneumonia in young children is very often accompanied or followed by severe intestinal disturbance. Mancini of the Infant Jesus Hospital at Rome, in the course of 200 autopsies on infants who had died of influenza, found that in addition to the broncho-pneumonia there was often a hyperplasia of the lymphoid tissue of the entire intestinal mucosa, and sometimes even a follicular colitis with ulceration which might be diffuse or limited to certain segments of the large intestine. In protracted cases the colitis was characterized by numerous areas of isolated or confluent ulceration, some of which were covered by diphtheritic exudation and accompanied by considerable oedema and inflammatory infiltration of the various layers of the mucosa and submucosa. Unlike Socin, who declared that there was a certain antagonism between tuberculosis and influenza, Mancini found that the greatest number of deaths from influenzal broncho-pneumonia occurred in infants aged from 1–3 years who showed previous tuberculous lesions, such as caseous tuberculosis of one or more peribronchial, peritracheal, and mesenteric glands. In children with tuberculous sclerosis of one apex or with tuberculous bronchitis or broncho-pneumonia in one or two lobes, influenzal broncho-pneumonia developed in its characteristic way, often assuming the confluent pseudo-lobar form.

Lucke and Barker studied the cellular composition of the pleural exudate complicating influenza in 17 cases, and found that endothelial cells constituted the predominant type of cell, especially in the early stages of influenzal pleurisy, while later they became gradually replaced by polymorphonuclear cells. The endothelial cells were slightly phagocytic for erythrocytes and occasionally engulfed bacteria.

Prophylaxis. Gregor, who had previously shown that workers in gas fumes present a certain amount of immunity during an epidemic of influenza (vide *Medical Science*, 1919, **1**, 50), has recently proved by experiments that groups of men can be exposed to $NO_2 + SO_2$ gases for lengthened periods during epidemic times without the slightest discomfort or harm. The nasal secretions after exposure to the fumes were found to be acid, and Gregor suggests that the mode of action of NO_2 and SO_2 fumes is to form an acid medium in the secretions of the upper respiratory passages which is inimical to microbial growth.

Orticoni, after alluding to Gregor's first paper, attributes the prophylactic value of gaseous disinfectants partly to their bactericidal action and partly to their forming a sort of mask which protects the upper respiratory tract from the penetration of micro-organisms. He states that in certain factories in the south of France where the workmen were exposed to the fumes of eucalyptus or products of eucalyptus during the last epidemic, the number of those attacked was very small, and no severe form of the disease was observed.

Meader, Means, and Hopkins found that the most effective measures for controlling the outbreak among the American troops in England was the prompt isolation of all men showing temperatures, and increasing the amount of space allotted to each man. There was no conclusive evidence that masking and prophylactic spraying was effective.

Salvat, Professor of Hygiene in the Faculty of Barcelona, uses a prophylactic vaccine similar to that of the British War Office, but containing in addition recently isolated parameningococci. The vaccine was used in about 5,000 cases, four doses being given of 50, 100, 150, and 200 millions respectively. In a group consisting of about 4,900 Spaniards there were no fatal cases of influenza or even of severe broncho-pneumonia, whereas, in a group of about 50 persons of British nationality there were five complicated cases and two deaths. Salvat attributes this to the fact that the illness occurred after the patients had left for another country, which proves that the vaccine should be prepared in the patient's own country. He also attaches some importance to the ethnic factor, certain races being more vulnerable than others.

Treatment. Meader, Means, and Hopkins emphasize the importance of moving cases as little as possible, and getting them to bed with a minimum of delay. Long journeys in hospital trains they regard as distinctly inadvisable.

Black-Milne and Rogers treated 35 cases of influenzal broncho-pneumonia or pneumonia with the Army mixed **vaccine**, the formula of which is 30 million *B. influenzae,* 100 million pneumococci, and 40 million streptococci in 9 minims. The dosage used at first was ♏iii and later ♏v for the first dose, and ♏v and later ♏viii for the second dose. No bad effects were observed, the condition being not affected where it was not improved. Of the 35 cases 3 died. In the majority of cases the treatment was followed by improvement in the general condition and in the character of the sputum, and by a feeling of well-being.

Hughes treated 16 cases of epidemic influenza in the early stages of the disease with subcutaneous injections of polyvalent **antistreptococcus serum**. The initial dose was 10 c.c. repeated every 24 hours if the temperature kept up. In most cases there was a fall of temperature to normal after one or two injections. In no case was more than 40 c.c. required. He also treated more than 14 cases of epidemic pneumonia with the same serum, which was given subcutaneously in 11 cases and intravenously in 3 with 5 deaths (2 of the subcutaneous and all the intravenous cases). In the very virulent and fulminating pneumonias characteristic of the epidemic,the serum was disappointing.

Calcium chloride is warmly recommended by Coglievina in the treatment of influenza. The reason for his choice of this drug was the success which he had had from its use in severe cases of gas poisoning. He attributes the favourable results obtained to its antiphlogistic action. It has been found experimentally by Chiari and Januschke that pleural and pericardial effusions which are caused by many infections or intoxications do not occur after injections of calcium chloride. The dosage was as follows: one group of cases was given a tablespoonful of a solution 10 : 150 by mouth. The other group was given 5 c.c. of a 1 per cent. solution by subcutaneous injection twice daily. Usually 10–12 injections were sufficient. The highest number ever given was 20. Coglievina also gave urotropin by mouth in doses of 5 gm. daily, as he had found it most successful in the treatment of typhus cases a few years previously. The earlier the treatment was instituted, the better the results.

The treatment which was found most effective by J. and C. Regan for influenzal croup was the use of steam inhalations carried out in a small room, in which the saturation of the atmosphere with vapour could be carefully controlled. Poultices to the neck and morphia and atropin sulphate hypodermically were also used. Intubation which was tried in six cases aggravated the condition, as the pressure by the tube increased the congestion in the mucous membrane below, and so added to the mechanical obstruction. Lynah found that relief was afforded by hypodermic injections of epinephrin.

Harry has successfully treated more than 30 cases of post-influenzal sinusitis with a 1:2000 solution of collosol argentum used in the form of a spray or syringed into the diseased cavity twice or three times daily. The preparation is non-toxic, non-irritant and tunes up the nasal mucous membrane.

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DISEASES OF THE DUCTLESS GLANDS

Thyroid. In examination of 21,182 recruits Kerr found 4,693, or 21 per cent., with enlarged thyroids. 27 per cent. were classified as moderately or greatly enlarged, and 73 per cent. as instances of a small degree of enlargement. The enlargement was diffuse in 38 per cent., affected the isthmus only in 52 per cent., the right lobe in 5 per cent. and the left lobe in 4 per cent. Physical signs such as tremor, tachycardia, vasomotor instability of the hands and curved nails were found in a higher percentage of men with thyroid enlargement than without demonstrable changes in the gland, but the differences were not striking, and no definite conclusions could be drawn.

Like Brendel and Helm (vide *Medical Science*, 1919, **1**, 285), Kerr found that the incidence was highest in Washington and Oregon and lowest in California and Nevada. There was an area of endemic goitre largely confined to the Pacific North-west and shading off to the South and East. There was again a slight increase in Minnesota which should be considered as a part of the endemic goitre region adjacent to the Great Lakes.

Leiner records a case of intrathoracic goitre or struma profunda, i. e. a variety of goitre where there is no visible sign showing the condition of the gland. It occurs in from 6 to 7 per cent. of all goitres. Gravity is the chief cause of the condition, and many factors act as an adjuvant, such as respiration, coughing, swallowing, and arduous work requiring extension and flexion of the neck. A further cause is labour, especially a difficult one, owing to the fact that with the cessation of ovarian function there is a corresponding hypertrophy of the thyroid, and also owing to the action of straining during labour. Leiner's patient was a woman aged 34 who, in 1916 had an enlarged thyroid and all the other signs of Graves's disease. Three years later though exophthalmos, von Graefe's sign, tachycardia and tremor were present, the thyroid could not be felt. The diagnosis of intrathoracic goitre was made and confirmed by fluoroscopy which showed a rounded triangular shadow in the upper part of the mediastinum with its base upwards. There was no displacement of the trachea or oesophagus.

Some years ago Albeck came to the conclusion that a definite relation exists between the thyroid gland and the vomiting of pregnancy; he found that women with a large and soft thyroid never suffered from vomiting during pregnancy, whereas when the gland was small and hard, vomiting was bound to occur during pregnancy. Later investigations confirmed these observations. In 1,581 cases he examined the thyroid a day after confinement, obtaining at the same time data concerning the occurrence, duration, and severity of vomiting during pregnancy, as well as eliciting from multiparae information as to vomiting during earlier pregnancies. He classifies the condition of the thyroid gland according as it was (1) visibly and palpably enlarged, (2) palpably enlarged, (3) palpable, and (4) small. The following table shows the relation of the size of the gland to the incidence of vomiting:

	No. of Cases.	Vomiting throughout Pregnancy.	No Symptoms.
(1) Gland visibly and palpably enlarged	105	...	87·6 %
(2) Gland palpably enlarged	602	3.99 %	50·9 %
(3) Gland palpable	642	12.45 %	20·1 %
(4) Gland small	232	30.13 %	0 %

When the material was adjusted so as to show the relation of the size of the gland to the time at which the vomiting occurred, the following results were obtained:

	No. of Cases.	Vomiting in the 2nd to 3rd month.	Vomiting in the 1st month.	Incidence of other symptoms of short duration.
(1) Gland visibly and palpably enlarged	105	...	0·95 %	11·4 %
(2) Gland palpably enlarged	602	15·3 %	8·8 %	20·9%
(3) Gland palpable	642	39·2 %	9·0 %	19·6 %
(4) Gland small	232	50·5 %	9·9 %	9·5 %

Apart from the size of the gland, it was noticed that vomiting was rarer when it was soft than when it was hard. Information gleaned from multiparae concerning vomiting in previous pregnancies was correlated with the condition of their thyroid glands with the following results:

(1) Gland visibly and palpably enlarged: 48 cases: not a single record of vomiting during pregnancy.

(2) Gland palpably enlarged: 193 cases: of these 148 had never been associated with vomiting.

(3) Gland palpable: 79 cases: of these 50 had never been associated with vomiting.

(4) Gland small: 151 cases: every case associated with vomiting during earlier pregnancies.

Albeck has further studied the microscopic structure of the thyroid gland of 35 pregnant and 40 non-pregnant sows. In the latter the gland was composed of uniformly large follicles, separated from each other by narrow walls. Their lining consisted of short cubical cells. Here and there among the large follicles were groups of small follicles lined with tall, cylindrical epithelial cells. This was the structure of the gland in every one of the 40 sows examined, and in none were those features found which were demonstrable in the gland of the pregnant sow. Here, after the third or fourth month of pregnancy, there was great proliferation of the cellular elements. The follicles had apparently become more numerous, and were small and corrugated. The epithelial lining was often composed of several layers of cells, high and cubical or cylindrical. The structures separating one follicle from another were comparatively thick, and included well-developed connective tissue fibrils and capillaries filled with blood. These changes were most marked in the middle of pregnancy; they were no longer demonstrable at the end of pregnancy. Albeck has also compared the weights of the thyroid glands of pregnant sows and cows, with those of non-pregnant sows and cows, estimating the weight of the gland in relation to the total weight of each animal. There was no evidence of hypertrophy as a result of pregnancy.

Marañón describes a sign which he has found in 92 out of 100 cases of all forms of hyperthyroidism consisting in an erythema of the skin of the neck when it is gently rubbed with the finger. The erythema is more intense on the neck than in the adjacent parts, and when a goitre is present, may be limited to the skin over it, or if the goitre is unilateral it may be more intense on the corresponding side. The erythema may be uniform or irregular, smooth or accompanied by swelling of the skin. Marañón attributes the phenomenon to a hypersensitive condition of the vasomotor nerves caused by the excessive thyroid secretion or by a change in its quality.

In an article on the basal metabolism and hyperglycaemic tests of hyperthyroidism McCaskey states that Friedrick Müller and Magnus-Levy showed about 25 years ago that one of the most characteristic phenomena of hyperthyroidism was an increase in general metabolism while hypothyroidism produced the exactly opposite result. McCaskey now points out that the clinical application of basal metabolism or the metabolism of the fasting body in the resting stages may be used in the differential diagnosis of mild, atypical, or very early cases of hyperthyroidism. The average normal heat production which is an accurate index of metabolism is about 39·7 calories for men, and 36·9 for women. Physiological variations of not more than 10 per cent. may occur in either direction. In hyperthyroidism there is an increase up to 100 per cent. or more, according to the severity of the case and in the same case at different times.

In like manner Means and Aub of the Massachusetts General Hospital at Boston consider that the determination of basal metabolism is a valuable means of differential diagnosis in obscure cases of hypothyroidism. The methods employed consisted in the determination of the gas exchange of the recumbent subject while in the post-absorption condition by means of the small Benedikt apparatus and the calculation of the heat production therefrom. Basal metabolism determinations in untreated cases of myxoedema, cretinism and cachexia strumipriva showed a definite reduction below that of normal individuals of the same age and sex. The metabolism was brought to normal or above by the administration of thyroid extract. The writers are of opinion that the determination of basal metabolism is a far better guide as to the dosage of thyroid preparations in cases of hypothyroidism than the clinical symptoms. Doses of 3–4 grains of thyroid extract should be enough to bring the metabolism to normal in two or three weeks, and doses of from 1–2 grains daily should usually be sufficient to keep it there.

Lueders regards the sugar tolerance test as an important aid in the detection of border-line cases or early hyperthyroidism. In 5 out of 7 cases of exophthalmic goitre hyperglycaemia was present and in 2 of the 5 cases there was glycosuria. In 31 cases of hyperthyroidism examined by McCaskey, the blood-sugar content was increased within two hours, from 50 to 200 per cent. In 70 per cent. of the 31 cases the maximal rise occurred at the end of the first hour, with a more or less sharp decline at the end of the second hour after the ingestion of 100 gm. glucose.

In his thesis for the degree of Doctor of Medicine, Sölling has attempted to answer the question : What factors determine the morbid changes in the thyroid gland in Graves's disease ? In his study of 97 cases, he found a considerable proportion in which the onset directly succeeded an acute infectious disease. In 20 other cases exacerbations of Graves's disease, which had been for a considerable time stationary or even cured, coincided with the outbreak of an infectious disease. The demonstration of round cell infiltration in excised portions of the thyroid gland also suggested an inflammatory process. In 13 cases the disease began with a sore throat, which was either an isolated phenomenon or one of a series of influenza-like symptoms. In one case the sore throat developed during convalescence from a severe attack of typhoid fever. Sölling has also collected from the literature 42 cases in which an infectious disease preceded the outbreak of Graves's disease. In most of these cases the infectious disease was coryza, influenza, or rheumatic fever. The sore throat which often ushers in rheumatic fever is noteworthy in this connexion. In 7 cases tenderness and swelling of the thyroid gland coincided with the development of an infectious disease, and in 17 of the 20 cases of Graves's disease already referred to, the thyroid gland became larger, and in 10 it also became tender. The subjects of Graves's disease are particularly liable to contract infectious diseases of the throat, and while 60 of the 97 cases showed this tendency, it existed in only 23 out of 100 women. In 62 of the 97 the enlargement of the thyroid was at first limited to only one portion of the gland : and from this original focus the swelling extended to other portions or to the whole of the gland. In 40 cases the isthmus was the portion first affected, in 15 cases the base of the right lobe. Infection of the gland, if it does occur, must travel by the lymphatics or blood-vessels. The fact that the disease usually starts in the isthmus or base of a lobe, hardly ever in the upper portions of the gland, points to lymphatic infection. In the chapters dealing with the pathology of the thyroid gland, Sölling shows that the clinical and histological manifestations of subacute thyroiditis and Graves's disease present so many features in common that the one merges into the other without the possibility of a hard and fast line being drawn between them. Discussing the mechanism of exophthalmos, Sölling bases his explanation on Landström's investigations into the innervation of the smooth muscles of the orbit by the sympathetic. The structure and position of these muscles are such that their spasmodic contraction induces exophthalmos as well as the other ocular manifestations of Graves's disease. Hence the conclusion that these manifestations are the expression of irritation of the cervical sympathetic. The abundant connective tissue about the thyroid gland is probably the site of an inflammation affecting the cervical sympathetic; and in both the cases observed by Sölling, in which the enlargement of the thyroid was confined to one side, the ocular symptoms were confined to the same side. In 39 cases in which one side of the thyroid was more enlarged than the other, the severity of the ocular symptoms was correspondingly greater on that side. They were equally severe on the two sides when the enlargement of the gland was diffuse, 2 cases excepted. In 2 cases in which recovery had practically been effected after operation, the ocular symptoms having vanished, a relapse followed (one after a sore throat), and the eye that became most prominent corresponded with the side on which the gland became swollen. In several cases in which one side of the gland was excised, the diminution of the ocular symptoms was most noticeable on the same side, and as exophthalmos is the last symptom to disappear, the longer a case is observed after operation, the greater is the difference between the ocular symptoms on the two sides. When, as often happens, the exophthalmos persists after operation, the post-operative formation of scar tissue may be responsible for the continued signs of irritation of the sympathetic. In cases of Graves's disease without exophthalmos, the sympathetic has presumably not been involved in the proliferating, periglandular connective tissue.

Of the 97 cases 83 were operated on, the remainder being treated by more conservative methods. Seven of the 83 are excluded from the rest as the diagnosis of Graves's disease was challenged. Sölling has also collected, for the purpose of comparison, 75 cases for which only conservative treatment was prescribed. The observation period (after discharge from hospital) was 10 to 3/4 years for these cases, 5½ to 3/4 years for the cases operated on. The results were the following:

	Conservative Treatment.	Operative Treatment.
Perfectly cured	15	45
Much improved	8	11
Myxoedema	1	—
Unaffected or relapsed	32	6
Died of Graves's disease	19	—
Died in connexion with the operation	—	11
Died some time after the operation	—	3

Four of the operative deaths should, however, be excluded, as the patients were moribund before operation. Though the comparison favours operative treatment, the mortality attaching to it is heavy and indicates the necessity for more scientific selection of cases for operation. In this connexion Sölling distinguishes between acute and chronic cases. The acute form often terminates fatally and early. Conservative treatment being comparatively futile, the care of the patient should be committed to the surgeon with whom the choice of time at which to operate should rest. In the slight form of chronic cases, the pulse being usually under 100, and the heart not being dilated, conservative treatment should first be given a trial for a year. Then, in the absence of definite improvement, the case requires operation, and the more strenuous the work awaiting the patient, the earlier should be the operation. The severe and the moderately severe cases, with a pulse up to 120 and slight cardiac dilatation, should at once be referred to the surgeon. Sölling emphasizes the importance of early diagnosis, and he deplores the fact that in many cases the diagnosis is not made till late in the disease. Tachycardia, enlargement of the thyroid and exophthalmos may all develop comparatively late or be overlooked for some time, and Graves's disease should always be suspected when lassitude is combined with rapid emaciation in spite of a normal or even voracious appetite.

Bergh, who has practised massage of the naso-pharynx for about 25 years, finds among his 11 cases of Graves's disease treated by massage much evidence confirming Sölling's views on the origin of this disease. Bergh's cases, the first of which dates from 1900, are as follows:

(1) A married woman, aged 38, developed, soon after her first confinement, influenza with violent pain in face, neck, and arms. Soon afterwards slight enlargement of the thyroid was noticed. She bled readily from the nose, breathed often through the mouth, and was troubled by a dry cough. The mucous membrane of the nose was very red and swollen, the pharynx was much inflamed, the tonsils were soft and enlarged, the retro-nasal space was oedematous, and there was much adenoid tissue between the tonsils and tongue. The size of the thyroid was reduced by a half when she was discharged after 42 sittings. The complete recovery was maintained during an observation period of 5 years. (2) An unmarried woman, aged 39, developed a goitre after she had suffered for years from naso-pharyngeal catarrh, sometimes accompanied by bronchitis. No benefit from treatment. (3) An unmarried woman, aged 18, had suffered from a protracted and violent 'cold' just before the development of Graves's disease. There was marked catarrh of the pharynx, the retro-nasal space was oedematous, and a pharyngeal tonsil was much enlarged. Rapid and complete recovery followed massage (25 sittings) and was maintained during an observation period of 16 years. (4) An unmarried woman, aged 27, suffered from marked rhino-pharyngitis and nasal obstruction. The recovery effected after three courses of massage (63, 13, and 33 sittings) was maintained during an observation period of 16 years. (5) An unmarried woman, aged 45, was very subject to nasal catarrhs and sore throat, and she suffered from severe pharyngitis. The tonsils were small, but the lymphatic tissue below them was much hypertrophied. The improvement effected by massage was maintained for 8 years, after which an attack of influenza was followed by a relapse. (6) An unmarried woman, aged 22, had suffered for years from catarrh of the naso-pharynx. She was a mouth-breather, and the tissues in the retro-nasal space were oedematous. Recovery followed treatment, but myxoedema developed 9 years later. (7) A married woman, aged 31, had been subject for many years to sore throat and a dry cough. There was rhinitis with pharyngitis, the retro-nasal space was oedematous, and the tonsils were enlarged. Recovery followed massage, but myxoedema developed 12 years later. (8) An unmarried woman, aged 27, developed Graves's disease after a severe fright. There was catarrh of the naso-pharynx and the tonsils were much enlarged. The marked improvement which followed massage was not maintained, a sore throat being followed by a relapse of Graves's disease. (9) A married woman, aged 48, had always been subject to colds, and had for some time suffered from a dry cough, most troublesome in the prone position. There was naso-pharyngeal catarrh, and the tonsils though small were very sensitive, violent coughing being provoked when they were touched. Improvement followed a short course of massage. (10) A married woman, aged 28, contracted scarlatina at the

age of 15, the nose and throat being severely inflamed. After this, the thyroid was enlarged for some time. She became subject to 'colds', the tonsils became enlarged, the naso-pharynx oedematous, and respiration became oral. Improvement followed a short course of massage. Later, a 'cold' was succeeded by a relapse of Graves's disease. (11) A medical man, aged 63, suffered from severe rhino-pharyngitis and oedema of the naso-pharynx. Only slight and transitory improvement was effected by massage.

Bergh gives very full details of all his cases with a view to proving that the development of Graves's disease was the outcome of a thyroiditis starting as an infection of the naso-pharynx, with propagation via the lymphatic system. If this explanation of the genesis of Graves's disease be correct, treatment should be confined (1) to removal of so much of the gland that the effects of its hypersecretion are discounted, or (2) to the condition of the naso-pharynx. Bergh prefers the latter alternative. For operative treatment is often fatal, has often to be repeated (of Sölling's 76 cases operated on, 17 had 2, and 3 had 3 operations) and it entails a protracted convalescence. If the naso-pharynx can be restored to health, as Bergh maintains it can by massage, then the source of constant new infection is cut off, and the inflammatory reaction in the thyroid subsides as it rapidly neutralizes the toxins already present. The average number of sittings necessary is 35. If no improvement is observed after 10 or 12 sittings, the massage should be abandoned. The patient usually begins to feel better after the first 6 to 8 sittings.

Sajous considers that all cases of exophthalmic goitre are due primarily to some toxin originating from a pathological process in one or more organs, such as the tonsils, sinuses, nose, naso-pharynx, teeth or gums, stomach, intestines, genito-urinary organs, nervous system, &c. Even the cases due to emotional stress in his opinion have as their primary cause toxic products formed in the cerebrospinal neurons subjected to stress, e. g., cholin, phosphoric acid and particularly neurin, a highly poisonous waste product. These poisons, by exciting the thyroid apparatus to supranormal activity cause it to secrete excessively, thus producing an additional toxicosis. The thyroid hormone, particularly when produced in excess, taking part also in tissue katabolism, breaks down fats including the fatty bodies in nerve and brain cells, thus accounting for the nervous phenomena of the disease.

Harvier points out that familial and hereditary Graves's disease was first described by Morell Mackenzie in 1868, who reported cases of two sisters with exophthalmic goitre, one of whom had two children similarly affected. Since then other examples of familial and hereditary Graves's disease appearing in childhood have been recorded by Solbrig (1870), Cantilena (1884), Osterreicher (1884), Kronthal (1893), Baylac (1896), Dubrueil-Chambardel (1907) and Railliet (1914). Examples of the condition occurring in adult life have been reported by Thysen, Rivalier (1889), Peter (1890), Raymond and Sérieux (1892), Dieulafoy (1893), Sottas (1896), Meige and Allard (1900), Schulmann (1917), and Souques and Lemaire (1918) (vide *Medical Science,* 1919, **1**, 224). Harvier relates a case in a man aged 19, in whom signs of Graves's disease developed in childhood. His mother, maternal grandmother and aunt, and a paternal aunt were similarly affected. The disease may appear at a very early age. In one of Dubrueil-Chambardel's patients all the signs of the disease were present at 4, and in Railliet's patient at 7 years of age. Harvier's patient showed tremor at the age of 3 years and enlargement of the thyroid at 12. The date of onset of the exophthalmos was unknown. In Schmauch's case the infant, which was premature, presented exophthalmos 5 weeks after birth. As a rule the disease is transmitted by the mother, but in a few cases the father alone is affected. In Harvier's case there was a history of the disease on both sides. Hereditary exophthalmic goitre develops without obvious cause. It does not seem justifiable to attribute all the cases to syphilis, as Schulmann is inclined to do. In some cases the symptomatology is complete, while in others the exophthalmos and tachycardia are more or less marked, but tremor may be absent (Kronthal) or disappear.

Loeper draws attention to the frequency of flatulent dyspepsia in Graves's disease, for which he suggests the following explanation. The meteorism is attributable to aerophagia caused by a spasm of the lower end of the oesophagus, as is proved by radioscopy. The spasm is the result of an abnormal excitability of the vagus which is also exemplified by the exaggeration of the oculo-cardiac reflex in Graves's disease. A proof of this mechanical origin of the dyspepsia is furnished by the fact that the condition can be cured by nerve sedatives, such as douches, baths, valerian, bromides, belladonna and rest.

According to Blondel the recent increase in sterility among women in France is due to the multiplication of cases of Graves's disease, one of the most frequent results of hyperthyroidism being atrophy of the uterine muscle, which is a great factor in sterility, even if the uterine rhythm is not affected. Owing to the antagonism between the thyroid and the thymus Blondel recommends in addition to local treatment of the uterus, the administration of raw thymus in the form of half a lamb's sweetbread a day, this being cheaper and quite as active as calf's sweetbread. It can be made up with flour, butter and salt into rissoles and taken in soup.

Bram considers that operative treatment of hyperthyroidism both in military and civil practice is not only unsuccessful but shocks and devitalizes the subject, and unnecessarily postpones the institution of successful non-surgical measures. In the absence of a pre-existing simple goitre and of pressure symptoms, or of malignant changes in the thyroid, he considers that practically every case of exophthalmic goitre is curable by properly directed dietetic, hygienic, medicinal, electrotherapeutic and psychotherapeutic measures, if persisted in with patience, skill and diligence for the proper length of time.

After alluding to his previous paper (vide *Medical Supplement*, 1919, **2**, 28 *b*), and the confirmation of his observations by Assmann (*ibid.*, 176 *b*), Zondek (1) points out that in myxoedema in addition to bradycardia and sluggish contractions the heart, and frequently also the aorta, show more or less dilatation. In the electrocardiogram the auricular waves and oscillations are absent, but only in normal contractions of the ventricle and not in extra-systoles, and under thyroidin treatment they reappear. The cardiac dilatation subsides and only the dilatation of the aorta persists. This cardio-vascular syndrome is often the guide to the diagnosis of abortive forms of myxoedema.

Zondek reports a case of traumatic myxoedema caused by a wound in the neck in which the characteristic abnormalities developed in the heart and electrocardiogram and soon disappeared under thyroidin treatment, thus affording an experimental proof of the specific character of these phenomena. When the waves in the electrocardiogram become abnormally high in the course of thyroidin administration, interruption of treatment is indicated, otherwise it should be continued. Other disturbances of the glands of internal secretion, such as acromegaly, infantilism, eunuchoidism, dystrophia adiposo-genitalis, giantism, osteomalacia, and hypoplasia of the ovaries do not show any peculiarities in the heart or electrocardiogram.

Benard reports a case of sporadic haemophilia manifested by recurrent epistaxis and delay in the coagulation of the blood in a man aged 24, the subject of myxoedema. After a fortnight's treatment by thyroid opotherapy the epistaxis ceased and the coagulation time became shortened. Benard refers to about 20 other cases on record of haemorrhages associated with thyroid insufficiency which have been successfully treated by thyroid opotherapy. The effect of the treatment is due to its action on calcium metabolism, though it is uncertain whether it acts directly or by the parathyroid.

Ransom considers that the action of iodides in relieving a condition in which the thyroid secretion is deficient is due to two facts: (1) iodine is specifically absorbed by the gland; (2) the iodine in the gland in saturating the unsaturated fatty acids of the blood-supply favours the autolysis by which the active principle of the gland is produced. The efficacy of the iodides in tertiary syphilis may be thus explained, and Ransom suggests that tertiary syphilis may be successfully treated with thyroid.

Suprarenals. Sézary adopts the following classification of the forms of suprarenal insufficiency: (1) fulminating form, (2) syndromes of suprarenal insufficiency with an acute, subacute or chronic course, (3) monosymptomatic form manifested by myasthenia or amyotrophy. The fulminating form is characterized by the occurrence of sudden death, often without any occasional cause, and sometimes after a surgical operation. It is generally due to a destructive lesion of the suprarenals which in most cases is due to tuberculosis and occasionally to cancer. As Sergent has shown, this form possesses considerable medico-legal importance. The acute form of suprarenal insufficiency described by Sergent and Bernard, may occur as an isolated phenomenon in the midst of apparently good health, or develop in a subject who is already suffering from some infection or intoxication. In the former case the clinical picture may be that of acute poisoning or suggest peritonitis, appendicitis, meningitis, an apoplectic stroke or sudden coma without definite cause. Anatomically the syndrome is almost always due to a chronic change in the suprarenals (caseous tuberculosis, occasionally cancer or sclerosis), which has remained latent for a long time and then suddenly manifested itself usually after some occurrence which would have had no effect in a healthy individual, such as a physical effort or a mild infection or intoxication. On the other hand, when a severe infection or intoxication is complicated by a suprarenal lesion the signs of suprarenal incompetence are masked by those of the causal disease. The symptoms as a rule in such cases are extreme adynamia, collapse and cardio-vascular weakness. *Post mortem* recent lesions of acute inflammation of the suprarenals are found. Much less frequently chronic lesions are discovered which have been roused into activity by the infection or intoxication. The protracted form includes not only typical Addison's disease but also the incomplete form to which Bonnet has given the name of 'Addisonism'. Sézary also describes an amyotrophic form characterized by a diffuse amyotrophy which is not explained by any nerve lesion and may be so pronounced that the patients are often supposed to have polymyositis or polyneuritis. There is also a subacute form of suprarenal insufficiency characterized by muscular weakness without amyotrophy and differing from Addison's disease in the absence of bronzing, and in its more rapid course. The anatomical lesions, however, are the same, and consist in slow and progressive destruction of the suprarenals by tuberculosis or cancer, and sometimes, especially in the amyotrophic forms, by sclerosis. The monosymptomatic forms of suprarenal insufficiency are the myasthenic form which resembles myasthenia gravis and the amyotrophic form which is of slow onset and may last 13 to 20 years.

The importance of suprarenal insufficiency in the pathology of war is discussed by Agnel. Its chief causes are overwork, wounds and infections of various kinds, of which the most important are enteric fever, bacillary dysentery, malaria, tuberculosis and various intoxications such as food-poisoning, alcoholism, chloroform, arsenobenzol, antityphoid and cholera inoculation and gas poisoning.

Loeper (2) describes a suprarenal dyspepsia which is characterized by gastric atony as shown by radioscopy and by obstinate constipation. There is discomfort rather than pain which occurs half an hour to two hours after food. In rare cases the dyspepsia is complicated by attacks of abdominal pain, nausea, and meteorism. Loss of flesh is very pronounced and rapid. Gastric analysis shows a diminution of free hydrochloric acid. The condition is curable by subcutaneous injections of adrenalin in doses of 1 and 2 mgm. two or four times in the 24 hours. Given by mouth the drug has no effect, probably owing to its neutralization by the digestive juices and especially by the liver.

McCarrison describes the effects of a scorbutic diet such as crushed oats and autoclaved milk on the adrenal glands of guinea-pigs. The naked eye changes consisted in enlargement of the glands with increase in their weight to nearly double the normal. The histological changes were haemorrhagic infiltration and disintegration of the cellular elements of the cortex and medulla. The changes occurred in animals which showed no clinical evidence of scurvy during life, and were regarded as pre-scorbutic in character. Although the weight of the organs was more than twice as great, the total quantity of adrenalin in the two glands in guinea-pigs fed on a scorbutic diet was less than half that present in healthy guinea-pigs.

In connexion with McCarrison's researches it is interesting to note that Byrne in carrying out autopsies on prisoners of war in German prison camps found that in a series of 8 cases of death from under-feeding the adrenals were definitely enlarged almost to half as large again as normal. The enlargement seemed to be mostly in the cortex on naked eye examination. There were no facilities for microscopy. Byrne suggests that the adrenals had hypertrophied to counteract the low blood-pressure produced by insufficient nourishment.

Bittorf describes the first case on record in an adult man of suprarenal tumour associated with atrophy of the testes and changes in the sexual characters. The patient was a man aged 26 who had noticed enlargement of the breast for the last seven months followed by atrophy of the testes, decline in sexual potency, and within the last month by the appearance of a tumour in the left flank. There were slight pigmentation of the face and rise of blood-pressure. Death was preceded by metastases in the liver and progressive cachexia. The autopsy confirmed the clinical diagnosis of hypernephroma which was of the cortical type.

Hypophysis. Strauss records the case of a woman aged 34, who for two years had had an enormously copious nasal discharge of thick, sticky, colourless mucus every three months, each attack lasting about three weeks. Dyspituitarism was shown by obesity, the absence of a desire for sweets, and the consumption of very little fluid. Application of adrenalin always aggravated the symptoms, while on the other hand treatment by small amounts of whole pituitary gland preparations had a favourable effect upon the hydrorrhoea in a few days, and the continuance of the treatment checked the discharge in two weeks. At the time of writing the patient had remained free from attacks for six months.

Lereboullet alludes to a case of diabetes insipidus reported by him five years ago in which the symptoms were temporarily relieved by subcutaneous injection of the posterior lobe of the hypophysis. Since then many other similar cases have been published showing that diabetes insipidus is often the direct or indirect manifestation of a change in the hypophysis which can be benefited by such treatment. Its action, however, is only transitory and rarely lasts more than twenty-four hours. The treatment therefore does not modify to any extent the prognosis of diabetes insipidus. It cannot remove the causal lesion or render aetiological treatment unnecessary, e.g., when the condition is due to inherited or acquired syphilis. It does not prevent a subsequent operation which is always serious and often fatal. But its value lies in causing a temporary relief of the patient's symptoms. It dispels the intense thirst for a few hours, calms the nervous symptoms, and restores sleep. The treatment is quite harmless, so that daily injections of 1–2 c.c. of the extract of the posterior lobe may be continued for a long period, and will be found to have a favourable action not only on the diuresis and thirst, but also on the obesity, general condition, development of the genital system, and even on growth.

According to Goudal the adiposo-genital pituitary syndrome in the adult is characterized by (1) rapid and progressive obesity; (2) atrophy of the genital organs and disappearance of the sexual functions constituting late infantilism; (3) association of cerebral and visual disturbances. This triad of symptoms is sometimes accompanied by slight signs of acromegaly and frequently by diabetes insipidus. The diagnosis of the condition rests on the presence of the ocular signs, especially bitemporal hemianopsia, so that the patients are often sent to the physician by the oculist who finds other signs of the syndrome present. Lereboullet and Hutinel report two cases of the adiposo-genital syndrome in a man aged 33, and a woman aged 40 respectively. In both cases the ocular symptoms (bitemporal hemianopsia and double optic atrophy) and X-ray findings indicated involvement of the hypophysis. But whereas in the first case the pituitary lesion was primary and the genital symptoms and obesity did not appear till later, in the second case the exact chronology could not be determined as the ocular manifestations were not recognized until after cessation of the catamenia and the appearance of obesity. In both cases the thyroid could not be felt, and there was a myxoedematous thickening of the skin, but there was no doubt that the hypophysis was the gland primarily affected. The cause of the pituitary lesions is open to discussion. In addition to the numerous cases where a new growth is responsible are cases where an inflammatory change of infective origin is the cause, such as inherited or acquired syphilis and tuberculosis. In the cases reported by Lereboullet and Hutinel the stigmata were scanty and inconclusive, but in the absence of any other cause they were inclined to incriminate inherited syphilis and adopt specific treatment. Thyroid and pituitary opotherapy was also indicated.

Reichmann reports two cases of pituitary tumour in a woman aged 36, and a man aged 51, who presented the following symptoms: a red bloated face, exophthalmos without any other signs of Graves's disease, bradycardia, myasthenia, general emaciation, oedema of the legs, slight glycosuria, no albuminuria, early arteriosclerosis, high blood-pressure without contracted kidneys, osteoporosis and curvature of the vertebral column. In the first case, which came to autopsy, an eosinophil adenoma of the hypophysis was found, and in the other the X-rays indicated disease of that organ. In both cases the symptoms of acromegaly were of a rudimentary character. The cause of the peculiar condition shown by the two cases is regarded by Reichmann as a functional disturbance of several glands of internal secretion with over-activity of the hypophysis and suprarenals and impaired function of the thyroid.

Thymus. Newton records a case of enlarged thymus gland in an adult aged 20, complicated by aneurysm of the aorta probably due to over-exertion. Improvement occurred at first after X-ray treatment, but subsequently became ineffective when the aneurysm became a controlling factor in the morbid condition. Death took place from rupture of the aneurysm. There was no autopsy.

As the result of their experiments, Park and McClure of Johns Hopkins University came to the following conclusions: (1) The thymus is not essential to life in the dog. (2) Extirpation of the gland does not produce any detectable alteration in the hair, teeth, contour of the body, muscular development, strength, activity or intelligence of the experimental animals. (3) Extirpation of the thymus probably does not influence growth or development. The possibility that it may cause retardation in development and delayed closure of the epiphyses cannot be excluded absolutely. (4) Extirpation of the thymus probably produces no alteration in the organs of internal secretion.

Pluri-glandular syndromes. Mariotti reports a case of testicular dystrophy with definite symptoms of pituitary hyperactivity and thyroid insufficiency in a man aged 21. A portion of a healthy testicle removed from a man in whom total emasculation had been performed on account of epithelioma of the penis was grafted beneath the skin of the flank and was followed by a rapid improvement in the genital functions. The improvement, however, was confined to the genital sphere, and was of short duration. At the end of a year no trace of the testicular graft remained, and the patient's condition had become the same as before. Mariotti regards the failure of the operation as an additional argument for maintaining the pluri-glandular origin of these syndromes. In such cases it is best to treat the cause of the dystrophy, which in the present case was tuberculosis.

A case of pluri-glandular disturbance with predominance of symptoms of suprarenal insufficiency is described by Farmachidis of Genoa in a man aged 19. Melanodermia in various regions, leaden-coloured patches on the buccal mucosa and asthenia indicated suprarenal insufficiency, while involvement of the hypophysis was shown by polyuria. Owing to a history of venereal infection in spite of a negative Wassermann reaction mercurial treatment was instituted and complete recovery took place.

A pluri-glandular syndrome comprising suprarenal, pituitary and ovarian insufficiency associated with status lymphaticus and splenomegaly in a woman aged 33, is reported by Fici of the Institute of Medical Pathology of Palermo University. None of these glands of internal secretion was affected more than another, and the symptoms were of an attenuated character, but the result of their combination produced a rapidly fatal issue. The aetiology of the case was obscure. Tuberculosis could be excluded, and it is possible that distressing emotions may have been a factor.

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DISEASES OF THE BLOOD

The Blood in Health. Rothacker investigated the digestion leucocytosis in 30 men who were in average good health. He found that leucocytosis was apparent one hour after food, and reached a maximum two hours later. The increase varied from 800 to 3,000 white cells per c. mm. The differential count was not appreciably altered. He further noted that protein food always produced a leucocytosis while farinaceous foods were less constant in their action.

Lampe and Saupe discuss the increase of lymphocytosis in normal persons since the war. They consider that 20–25 per cent. was usual in pre-war days, while an average figure now is about 43 per cent.

They examined the blood of 50 normals and found that the total number of leucocytes was about the same as previously, the average being 9,329 and the extremes 16,167 and 4,967. The average lymphocyte count was 36·4 per cent. This has been attributed to antityphoid inoculation, to changes in nutrition, and to other factors. They do not feel that the matter is settled by any of these suggestions and are rather inclined to incriminate a functional or nervous factor.

Groll discusses the frequent occurrence of lymphatic hyperplasia in soldiers, but approaches the matter from a new point of view. He has not been able to carry out blood examinations or clinical work, and his investigations were made on material obtained at autopsies on those who had died of wounds.

Groll first deals with the question of how far antityphoid inoculation can be held responsible for lymphatic hyperplasia. In 264 cases he found only 26 per cent. of hyperplastic spleens, although the number included no one who had not been inoculated. He considers this to go far to disprove the theory of vaccine as a causal factor.

He believes that the lymphatic system diminishes in vigour as age advances and found his highest percentage of hyperplasias between the ages of 19 and 20, when 85·0 per cent. of casualties in healthy men showed enlargement of some or all of the tissues examined. Although many of these men had died of haemorrhage there were others who died of the effects of poison gas, and the only factor common to all is that they died speedily. Hyperplasia is never found amongst the ill-nourished, but rather the opposite change.

It is a remarkable finding that no less than 85 per cent. of young soldiers should be found to present a condition which has been called ‘status lymphaticus’ and which is characterized by indubitable hypertrophy of the lymphatic tissues. Groll supposes that this may as a matter of fact be a practically normal finding for that age and mentions that a lymphocytosis was not a very uncommon finding before the war, but was apt to be ascribed to some morbid condition not at the moment discoverable. In the same way slight degrees of polycythaemia had been spoken of as if they denoted definite diseases.

In connexion with the alterations in the leucocyte count which have been described as associated with war conditions, it is interesting to consider the normal count for different peoples. Colyer, writing of North Rhodesian natives, finds a very high proportion of lymphocytes. He examined 99 natives and the average count showed 55·3 per cent. with a polynuclear percentage of only 31·3. The eosinophil count was also high, namely 7·1 per cent. He compares these findings with those of chronic cases of malaria and finds them practically identical. From this fact and from the known universality of malarial infection amongst these natives he deduces that a normal count for them is the count of chronic malaria, and advises that this factor ought always to be kept in mind.

Fischer and Tsung have examined the blood of 115 Chinamen. Of these 75 were medical students in good health and living in good circumstances, while 40 were drawn from the coolie class. Both classes showed suspiciously high eosinophil counts, the former 4·6 per cent. and the latter 9·9 per cent. Other writers have reported similar percentages from China, and they contrast markedly with the maximum of about 3 per cent. met with in Europe and America. Fischer and Tsung attribute the eosinophilia to the very general presence of helminth infection of the intestinal canal.

Grober has investigated the blood in 79 natives of North Africa and compares the results with those of other writers. His attention has been especially directed to the red cell and haemoglobin estimations, to the specific gravity of the whole blood and of the serum alone, and to the refraction index of the serum and the percentage of dry residue of the blood. The first three of these run roughly parallel, but the specific gravity of the serum is more variable. It ranges from 1014 to 1041, to a considerable extent independently of the other findings. The index of refraction (compared to that of water) averaged 61·1 and showed no great variation, although rather on the high side of normal if anything. The dried residue averaging 22·2 per cent. varied, as one would expect, with the haemoglobin percentage.

The average red cell count was 6·2 millions, gardeners, who are classified separately, averaging higher than agricultural workers. Generally speaking, the different classes of workers did not show great variations. A certain number of suspiciously low counts are included which would suggest helminth infection, and this makes the average high count the more remarkable. There are six counts of eight million or over and one of 9,400,000. There are seven counts below five million.

The varying figures might apparently be explained to a large extent by the rapidly altering balance between intake of fluids and loss by sweating, &c., in hot climates.

Stepp comments on the fact that a great deal of attention has been given to the quantitative estimation of the nitrogenous bodies in the blood, but comparatively little to other substances. He set out to estimate the carbon content after removal of albumin, &c.

His method is given in detail, and consists of precipitation with phosphortungstic acid, evaporation to dryness, and then incineration of the residue. He had difficulties with the acid at almost every stage of the process, and admits that his results are not always concordant or capable of explanation. He examined the carbon content in cases of diabetes, non-febrile conditions, febrile conditions and nephritis.

The results are expressed in milligrams per cubic centimetre of blood, and the normal is estimated at about 175. Only in febrile cases and in diabetes was this figure much exceeded. Of six febrile cases the highest figure was 249 (meningitis and pneumonia) and the lowest, 197 (catarrhal pharyngitis). In diabetes a figure of 353 was reached. In this case and in two others the carbon residue was less than would have been expected from the known amount of sugar alone. Stepp recognizes that this seriously invalidates his method. Generally speaking, the figures for carbon were roughly normal plus the amount deducible from the known amount of sugar, so that the curves for sugar and for residual carbon run parallel.

According to Strassmann of the Berlin Institute for Instruction in State Medicine, comparatively little information is to be obtained from works on medical jurisprudence as to the putrefactive processes in the blood after death. The prevalent view seems to be that putrefaction of the blood takes place rapidly. Kratter maintains that the changes in the formed elements are most pronounced in the red cells in which they set in soon after death, and Kockel states that the leucocytes do not disappear till later. Before the publication of his present article Strassmann had found that these statements as to the early destruction of the red cells were not always correct. In two bodies which had been exhumed, one seven weeks and the other two months after death, he had been able to find a large number of easily recognizable red corpuscles and lymphocytes, but no neutrophils or eosinophils. He now reports a case in which red corpuscles in a good state of preservation were recovered 6½ months after death, as well as a few lymphocytes but no other variety of leucocytes, from the intrathoracic haemorrhages of a man who had been shot in the chest.

Bauer and Aschner employ a novel method for estimating the fragility of the red cells and attach importance to readings which are often given little consideration by other authors.

Their method, taking an experiment with salt solution as one example, is as follows. A series of tubes is filled with 3 c.c. each of varying strengths of salt solution and red cells are added as usual. A tube showing complete haemolysis is taken as a standard, and this is diluted until it matches in succession each of the tubes in which partial haemolysis has taken place. Taking complete haemolysis as 100 per cent. it is now easy to calculate the actual amount of haemolysis in each of the other tubes in percentages.

From the figures so obtained a curve can be constructed which admits of ready comparison with those from other cases. These curves also show the range over which haemolysis takes place, i.e. the interval between the point at which haemolysis is respectively absent and complete. Young red cells were found to be more resistant than old. This was determined by inducing a rapid output of young cells by phenylhydrazine haemolysis induced in a case of erythraemia. The range of haemolysis was found to be increased. As one would expect, the greatest range of existence was found in severe anaemias. The smallest range was found in tuberculosis, and this could be increased by tuberculin injections. Bauer and Aschner did not find this fact of value in prognosis.

Increased resistance was also found during menstruation. The paper is a long one and includes many cases and a consideration of the significance and value of the results obtained.

Aplastic anaemia. In three papers Parkinson gives the history of a case of acute aplastic anaemia which recovered. The case was seen and discussed by members of the section for the study of disease in children of the Royal Society of Medicine in July and November, 1918, and finally in August, 1919. This case seems to be unique.

The patient was a boy and aged 9 when first seen. He was suffering from a petechial rash, bleeding from the gums, and anaemia of about six weeks' duration. The tonsils were enlarged and a few glands could be felt in the neck, but the spleen and liver were of normal size. The red cells were 1,260,000, the haemoglobin 20 per cent., and the white cells 800 only, of which 72·5 per cent. were lymphocytes. No nucleated red cells but considerable anisocytosis, and poikilocytosis. Later the red cells fell to 624,000 but the white rose slightly to 1,600 per c.mm. 330 c.c. of citrated blood were transfused from one donor, and ten days later 550 c.c. from another. Both donors had been tested in the usual way. During this second transfusion the patient collapsed, and at the end of the operation there was epistaxis and an outbreak of purpura. He also passed blood by the rectum and in the urine, and had haematemesis and was deeply jaundiced. Evidently profound haemolysis occurred. The second donor developed influenza on the day following. The child grew weaker, had incontinence of urine and faeces, and was taken home to die.

The medical history of the patient at his own home is not given, but he seems to have made a complete recovery and was shown with a red cell count of 4,420,000 and haemoglobin 75 per cent. one year after the commencement of his illness. There was no aetiological factor in this case that could well be considered of importance.

A second case recorded in Parkinson's third paper was fatal in three months. This patient had suffered from scarlet fever 18 months previously; the first case had had this fever two years before aplastic anaemia developed. In a third case mentioned in the discussion, scarlet fever seemed also to have been a possible aetiological factor. None of the cases had albuminuria. Parkes Weber supported a toxic origin of the disease, and suggested an analogy with trinitrotoluol poisoning in which an atrophic type of anaemia is characteristic.

Bernardi discusses the value of the terms pseudohyperplastic and pseudoaplastic and prefers the latter for the class of case which he describes.

The case is that of a man of 38 who suffered from an acute anaemia with few physical signs in about five months. The blood showed the characteristics of aplastic anaemia in some particulars but was also reminiscent of leukaemia in that there were 10 per cent. myelocytes. There was no leukaemic infiltration of the liver or kidney, so that the latter diagnosis cannot be considered. Contrary to expectation, the marrow was found to be actively erythroblastic and to present many abnormal forms which had been conspicuous by their absence from the blood-stream.

The case may be read as one of subacute haemolytic anaemia in which the marrow was unable to compensate for the injury to the usual extent seen in idiopathic pernicious anaemia, the lack of compensation being obvious in the atypical blood picture and in the small degree of siderosis found at autopsy.

The author gives a full discussion of conflicting views on these points.

Pernicious anaemia. Herzog discusses the question as to how one is to classify those cases which show the clinical picture of pernicious anaemia and yet lack some points in the characteristic blood picture. He differs from many German writers in concluding that Biermer's anaemia is to be considered as a haemolytic anaemia rather than myelopathic; in other words, he discards the primary marrow degeneration hypothesis on which so much work has been done. But he is not able fully to eliminate the marrow degeneration factor, for he admits that it may take a subsidiary place in causation, which place he does not define.

While admitting haemolysis as the predominant factor he does not feel able to agree with Hunter with regard to glossitis. He does not clearly differentiate between inflammation of the tongue and non-inflammatory atrophy which he considers to occur in many conditions other than anaemia, e.g. achylia gastrica. He thinks that pernicious anaemia may occur without any glossitis, although the latter is often seen. From the points of disagreement adduced he seems to hold Hunter responsible for the view that glossitis only occurs in pernicious anaemia and is never absent in that disease.

Herzog also dissents from the view that achylia gastrica is necessarily present in pernicious anaemia, and his two cases did not show this condition. Of these two cases the first had 83 per cent. of polymorphs, and the second 34 per cent. of eosinophils, so that there is prima facie evidence for their exclusion from the pernicious anaemia group, which tends to invalidate any argument based on the absence of achylia gastrica in these particular cases. The second had also a low colour index, to which attention is devoted, but the fact that he had several profuse haemorrhages from the bowel seems to have too little weight attached to it as a possible cause of the low index.

Finally Herzog is unable to come to any definite conclusion about his cases except that neither of them admits of definite classification.

In the course of the last seven years, in which he has studied about 50 cases of pernicious anaemia, Zadek has become convinced that there is considerable truth in the doctrine of the intestinal origin of many, if not all, forms of pernicious anaemia. This view is supported by the almost constant presence of gastro-intestinal symptoms, and especially the invariable occurrence of achylia gastrica, and the hypermotility of the stomach. As these symptoms are not nearly so frequent in other forms of anaemia, it is impossible to deny them some aetiological significance. During the last two years Zadek has subjected 17 of his cases to a treatment consisting of rest in bed, careful diet, injections of sodium arsenate and salvarsan, hydrochloric acid and animal charcoal by mouth, and washing out the stomach and bowel. By this method he was able to obtain remissions more rapidly (on the average in 6–8 weeks) than by any other form of treatment.

Friedenwald and Morrison have carefully studied the gastro-intestinal symptoms in 76 consecutive cases of pernicious anaemia. In 57 cases the gastric contents were examined, and in only 4 of these was there absence of achylia gastrica, while in 42 it was complete.

The findings are thus generally in accord with those of other writers. In the ensuing discussion there were not wanting speakers who would refuse to diagnose pernicious anaemia where there was no achylia gastrica.

Hansmann and Howard have examined the stools and urine in 27 cases of pernicious anaemia. Urobilin and urobilinogen were estimated by a spectroscopic method. There are always difficulties in collecting stools at regular intervals, and moreover the substances to be studied are liable to oxidation even in the laboratory, so that the results are such as to lead to broad conclusions and require considerable caution when interpreted with regard to individual cases.

The conclusions come to were as follows: (1) The evidence of abnormal haemolysis occurs first in the stools, second in the duodenal contents, and lastly in the urine. (2) An increase of the urobilin and urobilinogen in the urine and stools above 12,000 dilutions is a constant finding in pernicious anaemia during the period of remission. (3) The presence of even small amounts of urobilinogen in the urine is evidence of a probable pernicious anaemia in the absence of signs of biliary or hepatic disease. (4) A low red cell count with a low urobilin-urobilinogen percentage suggests an imminent remission. (5) A high red cell count with high urobilin and urobilinogen percentage portends a relapse.

Hansmann and Howard have also studied the nervous lesions of their 27 cases and found definite evidence of sensory changes, especially by vibration and two point discrimination tests in all but seven cases. Only a single case was definitely negative. This is in accordance with the findings of Woltmann and other recent writers.

Stockton records the case of a woman who first suffered from pernicious anaemia in 1899. She improved slowly for six years and her blood then became normal. She was kept under observation until 1918, when a relapse occurred which proved fatal through an intercurrent pneumonia. Achylia gastrica persisted throughout the illness.

According to Saltzmann the combination of kidney symptoms (albuminuria, casts, oedema, and disturbances of the secretion of urine) with pernicious anaemia is very common, but the interpretations of this combination are much at variance. Some authorities attach little importance to the combination, which they regard as more or less accidental, others suspect nephritis of direct responsibility for the development of the anaemia. The writer gives detailed histories of 11 cases of pernicious anaemia in which post-mortem examinations were made. In many of these cases there were clinical signs of renal disease, and in every case the necropsy revealed more or less extensive fatty degeneration of the renal epithelium combined with haemosiderosis. Compared with the changes in the renal epithelium, the changes in the glomeruli were slight. In every case there was an increase of the interstitial tissue. The writer is very cautious in drawing conclusions from his material, and he is sceptical as to the renal disease being the primary condition and the cause of the anaemia, or the two diseases as the sequel to a common factor. In only two of his cases was there a definite history of syphilis and alcoholism. In several of his cases arteriosclerosis was also found, and in two there were anomalies of the kidneys (cyst, small lipomata, hypernephromata, and structures suggestive of small fibro-sarcomata). These anomalies, as well as the arteriosclerosis, he is inclined to interpret as the expression of a general vital deficiency paving the way for the other morbid conditions found at death.

Anders maintains that transfusion of blood offers more for progressive pernicious anaemia than any other form of treatment. From the literature since 1910 he has collected 450 cases in which 1,084 transfusions were performed, including a successful case of his own. Of 362 cases in which the result of the procedure was given, 204 or 56·3 per cent. showed an initiation of remissions. The average number of transfusions per patient was 2·4 while the extremes ranged from 1 to 20 operations. Repeated smaller transfusions, e. g. 200–500 c. c., which were free from dangerous reactions gave more satisfactory results than single massive ones. Of 185 cases in which the method was mentioned, 172 were transfused with citrated blood. In Anders's own case—a man, aged 65, who had reached an advanced stage before the procedure was employed—the effects of the first transfusion were decided and lasted eight months. The second transfusion was equally satisfactory, the patient at the time of publication being able to attend to duties which he had not performed for 10 years.

At a meeting of the Breslau Medical Society, Minkowski reported two cases of splenectomy for pernicious anaemia. The first case was that of a woman, aged 40, who had been suffering from increasing weakness and pallor for 4 months. On admission to hospital, the haemoglobin was 33 per cent., the red cells 1,200,000, the colour index 1·4, the leucocytes 2,800, 55 per cent. of which were lymphocytes, and the blood-platelets 40,000. Anisocytes, macrocytes, poikilocytes, and megaloblasts were present. In spite of repeated injections of salvarsan which had had very favourable results in other cases, the condition became worse, there was a tendency to haemorrhages from the skin and mucous membranes, and the haemoglobin fell to 22 per cent., the red cells to 750,000, the leucocytes to 19,000, and the blood-platelets to 30,000. In spite of a long and difficult operation owing to adhesions of the upper pole of the spleen to the diaphragm, there was already an increase in the haemoglobin, leucocytes, and blood-platelets five hours after the operation. The following day there was a remarkable change in the blood picture. Every field showed normoblasts, the red cells numbered 110,000, the leucocytes 5,700 with 75 per cent., neutrophils and only 21 per cent. lymphocytes, and the blood-platelets 6,800. The haemoglobin gradually rose to 64 per cent. and the red cells to 2,000,000. In the second case, in which the patient survived the operation only 10 hours, the haemoglobin, red cell, and leucocyte count which before the operation had been 16 per cent., 534,000, and 1,700, half an hour after splenectomy rose to 22 per cent., 900,000, and 6,200. In the subsequent discussion Rosenfeld alluded to a case of pernicious anaemia in which splenectomy was followed by improvement, but death took place a year later.

The transitory character of the improvement following splenectomy for pernicious anaemia is also emphasized by Anders, who as the result of his personal observations and examination of the literature holds that the results hardly warrant the operation. He quotes Krumbhaar, who in a series of late results of splenectomy in 153 cases noted a mortality of about 20 per cent. Of 33 cases collected by Moffitt, 8 died immediately or not long after the operation.

Acute haemolytic anaemia. In a paper entitled 'Acute Haemolytic Anaemia' Ward gives an account of a syndrome not hitherto recorded. He describes one case seen by himself and another reported as an atypical leukaemia in America. Acute haemolytic anaemia is defined as the state which follows sudden widespread destruction of red cells while they are still in the circulation. In this sense it must be allowed to be present in blackwater fever and intoxication with red cell poisons of the benzol group, &c. The writer's case is peculiar in that it occurred without any of the usual antecedents, and that the destruction was apparently confined to the portal circulation, for although there was jaundice there was no haemoglobinuria.

The patient was a soldier. After a week's indefinite malaise he was noticed to be suffering from intense pallor and jaundice. He became rapidly worse from the clinical point of view, being delirious and collapsed and complaining of intense thirst. But the blood when first examined showed already an intense erythroblastic and myeloid reaction. The case was considered to be one of acute leukaemia until arrival at a hospital where more accurate investigation could be made enabled the writer to give a more hopeful prognosis. With the exception of an intercurrent pleurisy recovery was speedy and uneventful.

The American case referred to was also seen jaundiced and with an intense myeloid-erythroblastic reaction. He was treated by transfusion and died soon after.

The paper includes detailed consideration of the theoretical points and their practical bearing to which this case gives rise.

Leukaemia. Frøes calls attention to a simple staining reaction which may enable one to diagnose leukaemia with some confidence even if no microscope be available. It is based on the fact that the presence of a great number of white cells in a film leads to retention of sufficient of any blue stain to give a decided bluish tint to the smear. Frøes dissolves out the red cells by adding 0·5 per cent. hydrochloric acid to his stain. Even a well-marked leucocytosis gives but a slight reaction, while that of leukaemia is very definite.

In the case reported by Gasbarrini acute lymphatic leukaemia followed enteric fever after an interval of about two months. After an injection of antistreptococcic sero-vaccine there was amelioration of all the symptoms and rapid reduction of the number of lymphocytes. Improvement was not maintained. Gasbarrini discusses the possible uses of serum in leukaemia.

Tapie and Cassar discuss the different varieties of nervous lesion met with in myeloid leukaemia.

The first type is similar to the combined sclerosis sometimes seen in Addisonian anaemia. The symptoms may vary from ill-defined paraesthesias to paraplegia with incontinence and similar severe forms. Neither class is at all frequent in leukaemia.

The second type includes leukaemic infiltrations of the nervous system. These may affect either peripheral nerves, leading to deafness, facial paralysis or neuritis, or the brain itself. Treatment by X-rays may relieve the condition. An interesting illustrative case is given, that of a young man suffering from acute myeloid leukaemia fatal in less than three months. Seven days before his death he rapidly developed left-sided hemiplegia and became semi-comatose. At autopsy it was found that the internal capsule was the seat of a few minute capillary haemorrhages, while the whole of the nervous tissue was uniformly infiltrated with myeloid cells.

The third type is that due to haemorrhages into various parts of the nervous system, and it is obvious that it is not always possible to determine clinically whether such haemorrhages have taken place or whether one of the previous types of lesion is present. The manifestations to which such haemorrhages may give rise are many and variable.

The fourth type is that due to compression of nervous tissues by leukaemic infiltrations and is especially associated with chloroma.

The fifth type includes those cases in which herpes zoster occurs. This type is not uncommon. An illustrative case exhibited facial paralysis and herpes. The herpes was followed by intractable pain although the paralysis disappeared.

Baar and Kornitzer succeeded in isolating a Gram-positive streptococcus from the blood of a case of chronic myeloid leukaemia during life. The morphological and cultural characteristics are detailed. A history of multiple swellings of the joints would seem to require more consideration than it is accorded before the streptococcus can be held to be aetiologically related to the leukaemia.

Lewis describes the case of a boy aged 10, admitted to hospital with pain and discharge from the right ear. Associated glandular swelling led to the diagnosis of tuberculous mastoiditis. Operation disclosed a quantity of greenish-looking granulation tissue and a little pus. Temporary improvement was followed by death seven weeks from the apparent onset of the disease. The blood was that of a leukaemia characterized by excess of large uninucleate cells.

In an important monograph, Ricaldoni attempts a systematic classification of what are generally known as 'blood diseases'. He deals in particular with two groups. The first is that of primary lesions of the haemopoietic organs. This he divides into diseases with 'typical' lesions, i. e. lesions in which the proliferating cell is a true blood cell, and atypical lesions in which there is proliferation of endothelial or sarcomatous cells.

The group of typical lesions is sub-divided according to whether these are myeloid, lymphatic, or mixed.

The myeloid group includes three classes: (1) Erythrocythaemias, viz., the disease of Vaquez and Osler or Erythraemia or Polycythaemia rubra. (2) Leucocythaemias, viz., the two clinical forms of acute and chronic, each further divided according to the blood findings into leukaemic, subleukaemic, (Leukanaemia of Leube) and aleukaemic. (3) Erythroleucocythaemias, viz., Blumenthal's disease. Although Blumenthal described only a single case, others have since been recorded but are not noted by Ricaldoni.

The lymphatic group is divided into acute and chronic, each class being again divided according to the blood condition, as in the previous group. In the chronic group is included the pseudo-leukaemia of Pinkus, but the author evidently realizes that this is a wide term and that only certain cases will fit into his scheme. In the acute group is placed chloroma, with the recognition that any member of the group, whether subleukaemic or even aleukaemic, may show the characteristic green colour or bone lesions. Chloroma is not included in the myeloid group, in which Ricaldoni differs from many other writers.

The mixed group is included for the sake of completeness and is followed by a query. It is considered doubtful whether a true mixed leukaemia exists.

All the above are separated from a further group of typical lesions by the fact that they are generalized throughout the blood-cell forming organs. In a small localized group we find Kahler's disease and another form of pseudo-leukaemia of Pinkus.

There follows the second large class, viz., that of atypical lesions, and these again may be generalized or localized. There is only one generalized lesion, and this the endotheliomatosis of Gaucher's disease. In this as in many other points Ricaldoni reflects the more recent opinion on classification.

The localized atypical lesions include many diseases not commonly considered with the blood diseases in English literature but having obvious affinities. There are two sub-groups, the lymphosarcomas and the granulomas. The lymphosarcomas are single (lymphosarcoma of Virchow) or multiple (lymphosarcoma of Kundrat). The granulomas are described as (1) of the glands, (2) of the spleen, or (3) of the connective tissue. The granulomas of the glands include a malignant class, viz., Hodgkin's disease, the adénie of Trousseau, and also a further class which includes syphilis and tuberculosis. The splenic granulomas include an idiopathic splenic anaemia of infancy and of the adult and Von Jaksch's disease. Banti's disease is added as a third class. The author recognizes an affinity between leukaemia, leukanaemia, and the pseudo-leukaemia of Von Jaksch and Luzet, but finally classifies the latter as a granuloma.

The connective tissue granulomas are mycosis fungoides and Mikulicz's disease. It is recognized that syndromes resembling either of these diseases may occur in leukaemia.

The classification of splenomegalies is to a great extent elaborated in the above classification, but further details are given in another table. In this all chronic splenomegalies are divided into two classes, viz., the idiopathic or primary, and the secondary or those due to known causes. The latter group includes those splenomegalies associated with relapsing fever, malaria, kala-azar, syphilis, tuberculosis, infantile gastro-enteritis and rickets. These are infectious or toxic, but there is a further secondary group of spodogenous enlargements, i.e. those due to passive accumulation of waste, and this includes acholuric jaundice and also the splenomegaly associated with hepatic or biliary disorders.

The primary group of chronic splenomegalies contains the typical and atypical group diseases already mentioned, but those which are not generalized in other blood-forming organs are dealt with in rather more detail. The members of this group are divided into those diseases in which the lesion is peculiar to the spleen and those in which the lesion is not in its nature peculiar to any one organ but is most commonly manifested with a splenic localization. The former class includes only the spleno-sarcomatosis or sarcoma of the parenchyma described by Menetrier. The latter includes the ordinary form of lympho-sarcoma and the granulomas. The granulomas are divided again into (1) lymphatic splenic anaemia, (2) myeloid splenic anaemia, and (3) Banti's disease. The lymphatic form is of two varieties according to whether it occurs in infants or adults. The same is true of the myeloid form. When it occurs in infants it is the anaemia pseudo-leukaemica of Von Jaksch, and in adults the anaemia of Vaquez and Aubertin. Banti's disease is separated from adult splenic anaemia rather by its clinical features than on other grounds, although stress is laid on the sclerosing tendency of the process.

The above are the main points in Ricaldoni's classification, and it will be seen that it is more ambitious than that put forward by most authors and also less insistent on the varieties of lympho-sarcoma (e.g. chlorolympho-sarcoma, &c.) enumerated by German writers.

Hodgkin's disease. Harvier records three cases of Hodgkin's disease in which the pyrexia was so similar to that seen in undulant or Malta fever as to have given rise to doubt in diagnosis until the latter disease was eliminated by agglutination tests.

The first two cases were of the type in which this, the so-called Pel-Ebstein type of fever, commonly occurs. None of the external glands were enlarged, but the mediastinal and retroperitoneal formed large masses. In neither case was there any enlargement of the glands of the mesentery proper. The first case presented a rapidly developing collateral circulation through the abdominal cutaneous veins.

The triad of symptoms which justifies a diagnosis of this type of Hodgkin's disease is, according to Harvier, persistent relapsing pyrexia, splenomegaly, and anaemia.

The third case is introduced for comparison with the two former. It is that of a man of 31 who suffered from the classical type of enlargement of cervical, axillary, and other glands. To this was added a relapsing pyrexia, each relapse being accompanied by enlargement of the already palpable glands and the appearance of new ones. There was consequently no difficulty in diagnosis.

The symptoms suggesting Malta fever were relapsing pyrexia, profuse sweating, and, in one case, severe joint pains. Clinically the type of fever differs in that Malta fever is more regularly relapsing and each bout is of shorter duration than the last, while the intermissions are of definite duration and show an absolutely normal temperature. In Hodgkin's disease the periods of remission vary in length, may be relative rather than absolute, and may tend to eventuate in a prolonged intermittent fever which almost conceals the presence of relapses.

Cases of relapsing pyrexia in Hodgkin's disease occurring in soldiers have also been recorded by Abrahams, Howell, and Whittington. The abstractor (G. W.) knows of at least four unpublished cases, so that it would almost seem that this form of the disease has become more frequent. Abrahams adopts Osler's view that the recurrent pyrexia is due to an intercurrent infection, but Howell disputes this view, while Whittington instances his two negative blood cultures as evidence to the contrary. Howell's case had jaundice and so had Whittington's; in the latter case it was due to pressure of glands on the bile-passages. This case also had the unusual symptom of severe pains down the legs and was indeed admitted to hospital for this complaint. All three cases show how great may be the difficulty in diagnosis and how wide the difference may be even between different cases of this form of Hodgkin's disease.

A further case of Hodgkin's disease with relapsing pyrexia is described by Isaac. He states that this form is characterized by predominance of the 'malignant' process in the retroperitoneal and mesenteric glands and by the leucocyte picture, the diazo reaction, recurrent pyrexia, and cachexia. The liver and spleen are also affected. The case he has encountered presented a persistent muco-purulent diarrhoea as the earliest symptom. He regards it as a quite characteristic symptom, and at autopsy there was considerable thickening of the wall of the rectum. It is not stated whether the histology of this part showed the lesions of lympho-granulomatosis. He regards leucopenia as of definite assistance in diagnosis, but in his case periodic swelling of the cervical glands co-existed with the other symptoms and was of assistance in diagnosis. It is evident that the clinical picture regarded as characteristic by Isaac is not exactly similar to that described by McNalty and others in this country, but rather intermediate between the wholly 'latent or masked' form which closely resembles typhoid and the more usual glandular form. The temperature chart of Isaac's case, although showing undoubted relapses, is by no means a well-marked example of the Pel-Ebstein type of fever.

Lyon describes the occurrence of Hodgkin's disease affecting the mediastinal glands and causing pressure atrophy of parts of the sternum, clavicle, and ribs. Death was due to septic invasion of the exposed mediastinal tissues. There was also enlargement of abdominal glands, so that the case resembles those latent cases in which recurring pyrexia is often a feature. Lyon does not mention temperature, but from the history one may safely conclude that the Pel-Ebstein type was absent.

Haemophilia. Von Peters reports a case of haemophilia in a woman whose family history was as follows. The grandmother, mother, and an aunt on the mother's side suffered from severe menorrhagia but, except as mentioned below, from no other bleeding. The maternal grandfather had no haemorrhages, and died at the age of 89 from apoplexy. The patient's father died at 74 from aortic disease and never suffered from haemorrhages. Her mother suffered from heart disease which was fatal at the age of 64; latterly she had attacks of purpura. These took the forms of small petechiae such as one not infrequently meets at advanced ages and are not necessarily to be interpreted as signs of the haemorrhagic diathesis. Of the patient's six brothers, two suffered from nose bleeding and purpura, bleeding under the skin following slight injuries. There are no sisters. Her daughter is free from haemorrhages. The family suffers also from night blindness and colour blindness.

The patient was aged 42, of slender build. Menstruation commenced at the age of 13 and she suffered from well-marked chlorosis. At 25 her daughter was born; there was no excessive haemorrhage. In 1913 there was irregular but not profuse haemorrhage. In 1914 a cyst was removed from the ovary, and a fibroid uterus was removed. On the sixth day a large haematoma was found to have formed about the wound and the sutures had parted. The patient recovered from this.

The blood examination is reported. The platelets were 616,000 and the coagulation time by Wright's method 3 minutes 33 seconds. The other figures approached the normal.

The evidence of true haemophilia is thus not very weighty since other forms of haemorrhage of familial incidence are known, and the platelet count and coagulation time do not support a diagnosis of true haemophilia.

Orth, who reports a case of severe haemorrhage in haemophilia successfully treated by direct transfusion, states that the artery of the donor must be well-developed, and should be handled as little as possible at the time of the operation so as to prevent clotting.

Since 1907 Émile-Weil has treated seven cases of haemophilia by a prolonged course of injections of human or animal serum. One of the patients received as much as 30 injections in the course of six years, and others 20 or 12 without ill-effects. Six of the seven patients showed considerable improvement, the haemarthroses, haematomata, &c., completely disappearing. In the seventh case the improvement was less, and the haematomata did not disappear. Fever, slight pains in the joints, and urticaria occurred in some cases, but no serious anaphylactic symptoms were observed.

It has been shown that the state of anaphylaxis is associated with a hyper-coagulability of the blood. This was well exemplified in a case reported by Dufour and Le Hello, that of a girl with many profuse haemorrhages. Several injections of horse serum had failed of effect until she unexpectedly developed urticaria and other symptoms of the serum disease. The haemorrhages ceased forthwith. It would obviously be dangerous to induce anaphylaxis in patients in this manner, but a way out of the difficulty is provided by the work of Richet, Besredka, and others, who have shown that a state of passive anaphylaxis may be conferred on an individual by injections of small doses of serum from human beings or animals in the anaphylactoid state. The authors therefore set out to prepare such a serum, using rabbits that had been injected with many minute doses of horse serum. This they have employed in 16 cases of which notes are given. The results were most satisfactory, and it does not appear that they could have been due to any other therapeutic measures employed, or could have been effected in any other way.

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GONORRHOEA

Serum treatment. Since the first researches of Rogers and Torry, several observers have attempted to treat the different manifestations of gonorrhoea by means of subcutaneous injections of serum without much success. Debré and Paraf point out that a rational antigonococcic serum-therapy should introduce as early as possible an antigonococcic serum into the regions where the gonococci flourish. In the treatment of gonococcal arthritis, therefore, they recommend local injections into the affected joints. Their first experiments were made on animals. By injection of gonococci into the anterior chamber of the eye of a rabbit lesions were produced which were due to the action of microbial endotoxins. These lesions subsided after intra-ocular injection of antigonococcic serum 24 hours after the injection of gonococci, but were not influenced by subcutaneous or intravenous injections of the serum. Encouraged by this result they applied the treatment to human gonorrhoea, the best results being obtained in cases of gonorrhoeal arthritis, by direct injection into the joints. They remark that gonorrhoeal urethritis is not likely to be modified by local application of the serum to the urethra when the gonococci are buried in the urethral glands, and that vulvar, vaginal, and ocular gonorrhoea are also difficult to treat by local serum-therapy. The serum employed was prepared at the Pasteur Institute by Nicolle. Out of 15 cases of gonorrhoeal arthritis treated by this method, the results were favourable in 14. In 6 cases the symptoms subsided in 8 days; in 8 other cases before the 15th day. In one case only the treatment failed, in a pregnant woman in a very bad general condition. All the cases were recent infections; 11 male and 4 female, and nearly all had a urethral or vaginal discharge containing gonococci. The technique was simple; the affected joint was punctured and aspirated, and an amount of serum equal to or less than the quantity of fluid evacuated was immediately injected; compression was then applied to the joint. The injections were repeated two or three times, every day or every 2 or 3 days. In 6 cases 2 injections were given in the knee, wrist, and ankle; in 4 cases 3 injections were given in the knee; in 3 cases 4 injections were given and in 2 cases 5. In 6 of the cases the arthritis was polyarticular and the injections were given simultaneously in each joint. In 5 cases intramuscular injections of the serum were given in addition, and in 3 cases intravenous injections. Although these have no effect on the affected joints, they were given with the object of influencing the general infection and preventing the development of fresh lesions, in the same way that the association of intravenous with intraspinal injections has been recommended in the treatment of cerebrospinal meningitis. In 4 patients there was a local reaction, with pain and swelling of the joint, but this did not last more than a few hours. Debré and Paraf conclude that intra-articular injections of antigonococcic serum exercise a very favourable action in gonorrhoeal arthritis, provided the treatment is commenced in an early stage of the infection. The field of action is, however, limited to the larger joints, as it is impossible to inject the smaller joints of the fingers, toes, tarsus, and carpus when these are affected. With regard to the question of preparing different serums against the different varieties of gonococci, as is done in the case of the meningococcus, the authors state that such differentiation is, so far, not supported by their experiments.

In their paper on the **vaccine treatment** of gonorrhoea, Boas and Thomsen use the term 'prophylactic' in the sense of early treatment aiming at the prevention of complications, not of the local disease itself. They have used Bruck's and Reiter's vaccines, sold as 'arthigon' and 'gonargin', in many cases, and have found no benefits to counterbalance the febrile reaction and general malaise provoked. Earlier workers have usually adopted vaccine treatment for the complications of gonorrhoea; Boas and Thomsen have confined its use to early cases with a view to aborting complications. Their vaccine was prepared from 24-hour-old cultures on ascites-agar suspended in a 0·9 per cent. sodium chloride solution. The vaccine was always made from several strains of gonococci which were killed by freezing at a temperature of −15 for several days. Owing to the difficulty of counting gonococci, the strength of the vaccine was determined by comparing its density with that of a *B. coli* vaccine containing 1,000 million bacilli to the c.c. The injections were given at intervals of 5 to 7 days, the dosage of a series of 3 injections being 1, 1½, and 2 c.c. The reactions proving too violent, the dosage was reduced to ½, 1, and 1½ c.c. The injections were intragluteal, as for the injection of an insoluble mercury salt.

All the cases treated were ambulant, and males. In nine cases the injections were so painful that the patients refused to complete the course. The temperature was usually about 100·4° F.; in a few cases it reached 102·2° to 104° F. General malaise, headache, and giddiness were usual and vomiting was occasionally provoked. Only in one case was the reaction so violent that the patient fainted and was confined to his bed for a week. For the purpose of comparison, the records of 202 cases of gonorrhoea not treated with vaccines were collected, and, among these, 90, or 45 per cent., were complicated, about half of the total of complications being due to prostatitis. About a quarter was composed of cases of pure posterior urethritis, and another quarter of epididymitis. But among the 126 cases treated with vaccines there were only 23 with complications, i. e. 19 per cent. And this proportion could be further reduced if the 7 cases, which occurred simultaneously at a time when an inert vaccine was being given, be excluded. The 23 complications consisted of lymphangitis of the penis 1, periurethral infiltration 2, posterior urethritis 15, prostatitis 3, and epididymitis only 1. In one case epididymitis and prostatitis were combined. On the whole the complications in this class ran a milder course than in the case of the controls. But the vaccine did not appreciably affect the anterior urethritis, gonococci persisting in the discharge for the same period as for the controls. The duration of the disease was therefore not shortened except for the patients who would have developed complications but for the specific treatment.

Mercury in various forms has been tried by many observers in the treatment of the complications of gonorrhoea, and by gynaecologists in the treatment of salpingitis and salpingo-peritonitis, most cases of which are of gonorrhoeal origin. Bouveyron noted some years ago that intramuscular injections of **enesol** (salicylarsenate of mercury) given for syphilis also diminished the discharge from concomitant gonorrhoeal urethritis. He then found that intramuscular injections of enesol, given daily or on alternate days in doses of 6 cgm., had a favourable influence on the complications of gonorrhoea. He found enesol less painful and more effective than succinamide of mercury, which has been employed by several American observers. Without attempting to explain the mode of action of enesol—a compound of mercury and arsenic—he notes that arsenic in the form of intravenous injections of neoarsenobenzol has been shown to have a beneficial effect on gonorrhoeal urethritis and arthritis. In cases of gonorrhoea in which there is a free discharge, such as urethritis, cystitis, vulvo-vaginitis, and endocervicitis, the effect of enesol is less marked. Bouveyron hence concludes that this treatment is indicated in cases where the gonococci are in closed cavities. He especially recommends it in salpingitis, in preference to vaccines.

Lévy-Bing and Durœux, seeking for a means of attenuating the virulence and diminishing the duration of gonorrhoeal epididymitis, have employed intravenous injections of **arsenical compounds**, salvarsan, &c., which were found to give good results in gonorrhoeal rheumatism. For this purpose they used the new arsenical compound **sulfarsenol**.

After an experience with over 60 cases of gonorrhoeal epididymitis the authors claim that by this treatment the improvement in a week is as great as is usually obtained in three or four weeks by other methods. The number of injections was usually from three to five, given in doses commencing with 0·06 gm. increased up to 0·18 gm., and in severe cases up to 0·30 or 0·36 gm. Good results were also obtained in two cases of prostatitis, one of vesiculitis, and several of cystitis. The authors state that the other arsenical preparations may be equally effective, but that sulfarsenol has the advantage of less toxicity. As to its mode of action on the gonococcus, they incline to the view that the arsenical compound has a haemopoietic and tonic action which increases the power of resistance of the body.

Fogarty recommends treatment of acute gonorrhoea by the **massage-pack method**, which consists in packing the anterior urethra with gauze soaked in a solution of an antigonococcal drug. The drug preferred by Fogarty is a 5 per cent. solution of argyrol. The patient having passed water and the glans penis and prepuce having been washed with a 1 in 8,000 solution of potassium permanganate, a strip of gauze soaked in the solution is introduced into the urethra by means of a probe with a bulbous end. Having packed the anterior urethra the penis is gently massaged for five minutes, the pack is withdrawn, the meatus being gently compressed during the withdrawal to leave behind as much argyrol solution as possible. A second pack is then introduced and retained for four hours. Most cases are said to respond to two daily packings for four days, after which permanganate irrigations are given thrice daily. Fogarty claims that he only had 13 failures (7 uncomplicated and 6 with epididymitis, &c.) out of a total of 742 cases; but only 184 of these were tested by Gram staining of the smears. Of these 183 were negative after the fifth day. He regards this as the best abortive treatment of acute gonorrhoea.

Watson considers that **acriflavine**, in a 1 in 4,000 solution in normal saline, is the best drug to use for irrigation in gonorrhoea, and superior to permanganate of potassium, brilliant green, auramine, eusol, or chloramine T, all of which he has tried. In 196 cases of uncomplicated acute gonorrhoea treated in this way the average stay in hospital was 19·8 days, the actual treatment taking 15·4 days and observation 4·4 days. The complications arising during acriflavine treatment were few: two cases of epididymitis, two of subacute prostatitis, and three of cystitis. The treatment should be continued for at least 10–12 days, when the smear should be negative for gonococci, the discharge absent, and the urine free from pus or filaments. Cases which do not clear up in this time may be due to (1) cystitis from secondary infection; (2) cystic abscess or infected urethral ducts in the urethra; (3) prostatic or other glandular infection. Acriflavine is said to act in two ways: (1) by its gonococcicidal action; colonies will not grow on gonococcus medium washed with acriflavine; (2) by penetrating the mucous membrane and rendering it unsuitable for growth of gonococci.

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C. F. M.
C. L.

HYDATID CYSTS CONNECTED WITH THE BILE-DUCTS

There are two groups of cases in which hydatid cysts connected with the bile-ducts have given rise to a necessity for surgical interference. In the one the first thing noted has been the presence of bile in the peritoneal cavity, in the other the case has simulated obstruction by gallstones. It is urgently necessary that surgical treatment should be adopted before suppuration has supervened, and if steps are taken to remove the hydatid cysts the patient may be cured.

A. **Bile in the peritoneal cavity. Choleperitoneum.** Special attention was drawn to the subject by Dévé of Rouen in 1902; an extravasation of non-virulent bile into the peritoneal cavity results from the rupture of a hydatid cyst of the liver. The existence of the cyst in the liver may have been unnoticed beforehand. In several cases the patient has recalled that he had had a slight blow or squeeze in the liver region some time before the commencement of abdominal enlargement, but which was not severe enough to attract attention at the time. He may seek advice on the sole ground that the abdomen is enlarging, and the cause of this being found to be a collection of fluid in the peritoneal cavity, the diagnosis made before tapping may be that of ascites of obscure origin. If hydatids be suspected, and an X-ray examination be made, evidence pointing to the presence of a hydatid cyst in the liver may be discovered. The development of ascites may be attended by attacks of urticaria. A blood examination may reveal eosinophilia; also there is the serum-diagnosis, the deviation of the complement. When on tapping bile is found mixed with the peritoneal fluid, an abdominal incision is indicated in order to remove membrane and daughter cysts from the peritoneal cavity, as well as the parasitic lining membrane from the original cyst in the liver.

Dévé, after 1902, continued to add to the subject, and by 1918 he had collected 69 observations of what he termed 'choléperitoine hydatique'. He also described the following case, seen late and attended by complications, which proved fatal:

A man, aged 44, had suffered for six months from ascites of obscure origin. He had had no special symptoms, neither pain, nor urticaria, nor jaundice. Paracentesis abdominis had been performed several times, 8–10 litres of greenish fluid being removed. The fluid had rapidly re-collected—A median incision was made below the umbilicus, hydatid membrane and fibrinous masses partly free, partly adherent were, as far as possible, removed. Two holes, separated by a spur, were found leading into the liver and these were drained. There was an escape of bile and occasionally of hydatid membrane, until the original cyst in the liver refilled, then two hydatid cysts in each lung were found by the X-rays. Seven months after the first operation the refilled cyst was laid open from the convex aspect of the liver, some daughter cysts evacuated, and the cavity drained. Three weeks after the second operation the patient developed signs of an empyema at the base of the right pleura, but he opposed all further operation. A week after the discovery of the empyema, he threw up a quantity of foetid purulent material containing sloughs mixed with orange-coloured bile, but without hydatid membrane. The biliary fistula which had followed the first operation continued to discharge bile until his death. There was no post-mortem examination.

The longer the delay the more adherent becomes the hydatid membrane, because it is buried in fibrous tissue, mixed with bile pigments, and is intimately adherent to the intestine. Also daughter cysts multiply in the abdominal cavity.

Earlier and more active surgical treatment may bring about a cure as in the case reported by Anchütz:

A man, aged 32, previously healthy, after a fall upon the region of the liver, suffered from rapid distension of the abdomen. Four months later he was tapped and bile mixed with fluid removed. Thereupon the peritoneal cavity was laid open and the hydatids wiped out. Then bile and hydatids were found to be oozing from a rupture in the wall of the common bile-duct, and a large hydatid cyst was discovered on the convex aspect of the right lobe of the liver. This cyst was washed out and drained, and he was discharged four weeks after the operation with a small biliary fistula over the liver. Three months later he had to be operated upon for acute appendicitis, and the abdominal cavity being again examined, all the peritoneum was found to have returned to the normal, no more hydatids being met with. The biliary fistula, however, persisted for two months after the second operation, until the original cyst, then the size of a child's head, was removed from the convex aspect of the liver. Four years later the man had some more small hydatids removed from the gastrohepatic omentum and from the mesocolon in the region of the hepatic flexure. After this he remained sound.

B. **Hydatids obstructing the bile-ducts.** An acute obstruction may arise owing to a hydatid cyst of the liver bursting into the gall-bladder or bile-ducts. A chronic obstruction slowly develops and simulates obstruction by gall-stones. On exploration a small cyst is found blocking the escape of bile. It cannot be determined whether the hydatid cyst develops primarily in the hepatic duct, but the evidence points all that way.

Dévé collected 54 cases in which there had been long-continued biliary obstruction. There occurred intermissions in the intensity of the jaundice, which probably coincided with discharge of hydatid débris in the stools. Sooner or later grave complications had set in—suppuration in the gall-bladder, in the hepatic ducts, putrid gaseous suppuration in the original cyst, extending and setting up peritonitis or empyema.

Lecène and Mondor, in 1914, collected 30 cases of hydatid cysts in which there had been rupture into the bile-ducts. 20 recovered and 10 died.

Dévé described a case of chronic obstruction. A woman, aged 28, had had within the past year several attacks of jaundice, with pain in the epigastrium and occasional vomiting. Recently attacks of biliary colic had become more severe, necessitating relief by morphin. After seven attacks the wall of a ruptured hydatid cyst was found in the motions. In June 1911 the gall-bladder was exposed and found to contain a little seropurulent bile-stained fluid. The common bile-duct was distended with bile, but no calculus or hydatid membrane was met with. Bile continued to be discharged until the seventh day when a hydatid cyst, the size of a pigeon's egg, was found in the dressings. The patient recovered completely and eight years later was found to have had no return of pain or jaundice.

Another case of recovery was described by Fiolle of Marseilles. A woman, aged 37, had had an attack of jaundice 18 months before. The attacks had been repeated and generally lasted 20 days. She had pronounced jaundice, the urine was the colour of mahogany, the faeces whitish, the temperature about 39° C., the pulse about 80. There was moderate tenderness and fullness in the gall-bladder region. The gall-bladder was found not distended but the common and hepatic ducts very much so, and on incising the common duct thick, dark bile escaped. The duct was free down to the duodenum, and a drain was about to be inserted into the hepatic duct when a flaccid hydatid cyst was expelled, followed by a further flow of bile.

No sign of a hydatid cyst in the liver could be made out, nor did any more hydatids escape from the hepatic duct. After a temporary drain, healing was rapid, and six months later the patient stated that she had had no more trouble.

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W. G. S.

THE ACTIVE TREATMENT OF CUTANEOUS ANTHRAX

The active treatment of cutaneous anthrax is a subject at the moment in a state of confusion. This is evident from the selection of recent communications referred to below. The course taken by cases after apparently similar inoculations widely differ; there appears to be nothing in the earliest stages after infection to distinguish the case which will recover without any active treatment, from the case which will terminate fatally within a few days.

Early cases subjected to excision of the malignant pustule, or its destruction by the cautery, get a painful excavated ulcer which heals slowly and leaves an ugly scar. But this surgical treatment fails to check the course of severe cases. The cautery has been advocated in preference to the knife, in order that a protecting zone around the pustule may not be destroyed. Injections of carbolic acid or of perchloride of mercury into and around the pustule fail to arrest the spread in acute cases. It may be argued that such antiseptics do not destroy all the infective organisms, whilst they arrest the proliferation and kill the cells which are forming the protecting zone.

The active medical treatment is also a doubtful matter. A pessimistic view is that the patient produces his own antitoxin, which failing, his case is hopeless. The specific serums were considered inefficient until Sclavo prepared asses' serum. But it is stated that a non-specific serum, especially bovine serum, used freely, is as good, if not better than Sclavo's serum.

Trials have been made by treating the anthrax septicaemia by intravenous infusion of antiseptics—hypochlorite of soda, salvarsan, perchloride of mercury—but there is as yet an absence of evidence as to whether such a line of treatment is worthy of further trial.

In view of the number of cases of cutaneous anthrax which are being reported, e. g. inoculations from shaving-brushes, it seems urgently advisable that every case in which there are grounds for suspecting an inoculation should be immediately and freely treated with any serum which is at hand, whether it be Sclavo's serum or not. The extension of anthrax to the blood-stream must be anticipated. Provided there is treatment by serum at the earliest moment, surgical interference appears to be contra-indicated; the pustule will dry up and disappear without leaving a scar. The serum treatment should be continued until all induration has gone. In the severe cases, where the anthrax bacilli have reached the circulation, the treatment by large quantities of serum may perhaps be fortified by an intravenous infusion of an antiseptic—sodium hypochlorite or salvarsan. When no serum is obtainable for the moment, one or other of the above antiseptics should be injected without delay.

In 1917 Kraus and his colleagues in Buenos Ayres found that after being used for twenty years the specific serum of Sclavo remained a very doubtful remedy. The action of this serum was found to be very variable, as if the standardizing had been vague. Kraus first succeeded in obtaining regular results after inoculation by using guinea-pigs, animals relatively insusceptible to anthrax, and by selecting only small guinea-pigs weighing between 600 and 800 grammes. These were carefully dosed with virulent cultures, and then Kraus found that the normal serum of calves produced as good a passive immunity in his guinea-pigs as did the serum of oxen which had been already immunized against anthrax. Following upon this, normal bovine serum was found as active an immunizing agent as that from immunized oxen. Thereupon non-specific bovine serum was used for patients in doses of 10–30 c.cm., even 40 or 50 c.cm. being injected in intense cases. In a series of 50 cases no death occurred; among a second series of 96 cases there was one death, i.e. among the 146 cases of cutaneous anthrax treated with simple bovine serum in Buenos Ayres the death-rate was only 0·68 per cent. The ox serum was prepared by heating it twice to 56° C. for half an hour each time, by which any toxic effects were eliminated. It did not then cause serum sickness like horse serum. The non-specific serum was thought to produce a non-specific proteid reaction accompanied by a transient elevation of temperature and leucocytosis.

Hyman and Leary in the United States reviewed the treatment, and as compared with the results obtained by Kraus with simple bovine serum freely used, they found that the mortality of cases not so treated according to reports varied; the average mortality for cutaneous anthrax inoculated on the face was 40 per cent. They treated one severe case successfully with non-specific bovine serum, but their patient was not proved to have had anthrax bacilli in the general circulation.

Brown and Simpson reported on 25 cases among workers in a tannery in Massachusetts. There were three deaths. Excision proved less satisfactory than an expectant treatment, viz. a stimulating diet and perchloride fomentations.

Neve stated that in Kashmir anthrax was common and carried off thousands of cattle, a prophylactic serum not having been obtainable. Between 1900 and 1919 there had been 75 cases of cutaneous anthrax in hospital with seven deaths (9·3 per cent.); 40 per cent. of the pustules affected the upper extremities, 32 per cent. the head and neck, 12 per cent. the back, the remainder the chest, abdomen, and lower limbs. All occurred in males who had been engaged in skinning and cutting up animals dead of anthrax. The pustules might be single and large, up to 5 inches in diameter, or multiple up to six.

He burnt the pustule with a red-hot button cautery which encouraged local leucocytosis; excision and incision were considered dangerous as opening up fresh areas of absorption. When the anthrax became generalized the case was considered irremediable and hopeless.

Pijper reported from the Transvaal that salvarsan injection alone had been used in two cases. On a farm more than 20 of the cattle had died of anthrax. A white woman's hands came in contact with the blood of an animal dead of anthrax, and she developed a sore between the thumb and fingers. The next day the whole hand was swollen. On the third day the sore was diagnosed to be due to anthrax inoculation. 400 mgm. of salvarsan were administered by intravenous injection and the sore protected by dressings. The temperature became normal on the fourth day after the injection, and after some weeks of slow healing a slight scar only was left. At the same time a native on the farm scratched the back of his hand with a sharp piece of bone whilst cutting up an animal dead of anthrax. A pustule similar to the former case developed, and 600 mgm. of salvarsan were injected on the third day. The same result followed, the sore slowly healed.

Schultz noted two cases due to inoculation from a shaving-brush causing a pimple to start on the neck, but with an entirely different course in the two patients.

A man aged 23, after using a new brush for shaving, developed a pimple on July 14 which, on July 17, was diagnosed as cellulitis of the neck. An incision was made and subsequently anthrax bacilli were discovered. He died on the 18th from general infection by anthrax.

The second case, after using a new shaving-brush, developed a pimple on the neck on July 24. On July 27 anthrax was diagnosed. 50 c.c. of antistreptococcal serum were administered intravenously and sulphate of magnesia fomentations applied. The pustule was neither incised nor scraped. By July 31 he was recovering so that only a small depressed scar was left.

The presence of anthrax bacilli in the blood is generally a sign that the case is going to die. However, a patient who was actively treated by Graham and Detweiler, recovered.

A tanner aged 36 had been inoculated three days beforehand through an insignificant wound. A small itching pimple developed on the neck which was surrounded by vesicles containing brownish fluid in which anthrax bacilli were found. Induration of a livid colour developed around. 40 c.c. of anthrax serum were administered intravenously on the 3rd day, after that the indurated zone was injected with 40 per cent. alcohol. On the 4th day a wide excision of the pustule was made under a general anaesthetic. On the 5th day there was no improvement. On the 6th day anthrax bacilli were found in the blood. On the 7th day 100 c.cm. of chloramine T., Dakin, were administered along with 80 c.cm. of anti-anthrax serum. A rigor followed and then relief set in. On the 8th day bacilli were not found in the blood. There was slow healing of the wound and oedema persisted in the skin around for a good while.

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W. G. S.

SPINAL ANAESTHESIA

Surgeons who have the advantage of working in co-operation with special anaesthetists and with those trained by them are not much interested in the question of local anaesthesia. Yet a skilful combination of general and local anaesthesia may in some cases be advantageous; a sparing administration of the general anaesthetic after a minimal or subminimal dose of the local anaesthetic may suffice, e.g. to produce relaxation of the muscles of the abdominal wall, or when operations are being carried out in a hot climate. Particularly as regards the small amount of dose, spinal anaesthetics are superior to other forms of local anaesthesia. Under general anaesthesia are included the inhalation of nitrous oxide gas, ether, or chloroform combined with the inflation of oxygen or warmed air. Enthusiasts for local anaesthetics have helped out their action by administering beforehand, even overnight, veronal, scopolamin, morphin, omnopon, &c., in various combinations, to reduce the patient to a complicated state of narcosis, 'twilight sleep', &c., under which he must be much less safe than under a volatile anaesthetic. Those who have used these drugs, seem to be unacquainted with the skilful induction of general anaesthesia; they do not appear to know how a general anaesthetic may be administered so as to be sufficient for the particular stage of the operation, and yet not to affect the patient longer than the termination of the operation.

Of all the methods of inducing local anaesthesia, the spinal method is clearly the more suitable one to be generally adopted. It eliminates the necessity for making multiple punctures and the uncertainty attendant on attempts to inject sensory nerves outside the spinal theca and in the nerve plexuses; the objections to local infiltration are avoided, the artificial oedema owing to the quantity of fluid required, and the danger of necrosis because of the need for addition of adrenalin in order to reinforce the action of the other drugs.

In combination with a general anaesthetic, spinal anaesthetics may be used in small doses, and so possible dangers from injecting full doses are absent. When full doses are used the advantages claimed for spina anaesthesia must be subjected to a considerable discount. It is definitely contra-indicated in cases of shock and collapse, whether from injury with or without loss of blood, or from abdominal infections. There is set up by the spinal anaesthetic a fall of blood-pressure, the face becomes pale, and the tension of the pulse is diminished. When the patient has already been affected so that the blood-pressure is below normal, the additional fall may be a serious matter. Also in cases of high pulse tension, whether from arteriosclerosis, or in eclampsia, the sudden diminution from a high blood-pressure is dangerous and may cause the patient to faint. Then the recourse to stimulants neutralizes the anaesthesia.

The drugs generally used in spinal anaesthesia are stovain and novocain. Tropacocain is much more uncertain, and cocain, also holocain, may be said to be contra-indicated as too dangerous.

Eggleston and Hatcher placed the three former drugs among those rapidly eliminated, by the liver in particular, whereas cocain and holocain are much less rapidly got rid of. In the course of 300 experiments on cats they injected into the blood-stream, either a single poisonous dose, or fractions of minimal fatal doses, at intervals of 15–20 minutes. The more rapidly eliminated drugs were thus proved to be much safer, because although quickly absorbed, they were rapidly excreted; cocain proved dangerous, because, whilst as quickly absorbed, it was but slowly removed by the liver and kidneys. The addition of epinephrin exaggerated the difference in the rapidity of elimination between stovain and novocain on the one hand, and cocain on the other. The elimination of the former was increased, of the latter diminished.

All the local anaesthetic drugs killed the cats by a simultaneous arrest, both of the respiration and of the heart. Recovery from paralysis of both followed upon artificial respiration and squeezing of the heart, provided that immediately epinephrin was injected into a vein.

Meyer described the dangers of administering novocain in strong solutions and in full doses. Strong solutions of novocain injected subcutaneously in the regions of the head and neck may produce somnolence, from which the patient may be aroused but again relapse. This somnolence may last three-quarters of an hour and yet meanwhile there may be no complete analgesia.

Novocain when injected into a vein, even in such amounts as 5–7 cgm. of a 1 per cent. solution, may set up severe convulsions, epileptiform in character.

Injected in any way, subcutaneous, intramuscular, paravertebral, intrspinal, intravenous, a large dose of novocain causes collapse from fall of blood-pressure, cyanosis, arrest of respiration. When, after artificial respiration, the breathing starts again, there may then ensue for three-quarters of an hour a peculiar analgesia limited to the peripheral nerve endings.

Saphir, in New York, claimed for the double salt of quinine and urea chloride that it was an ideal local anaesthetic for rectal operations, because in 0·5 per cent. and 1 per cent. solutions an injection not only sets up local anaesthesia but the anaesthesia lasts from 10 days to a fortnight. The base of a pile, fissure, or fistula was injected with the solution until it turned white. The objection to the solution is that sloughing and slow healing is apt to result. If this is excessive death may follow. Thus H. J. Spencer described the case of a man aged 38 who had had external and internal piles for 10 years with bleeding and constipation. The piles were injected with the above solution and the same night he had a severe headache and shivered. On the 4th day there was pain in the right hypochondrium. On the 6th day there was septicaemia and pneumonia, a leucocytosis of 12,400, and the piles were sloughing. On the 7th day the liver and spleen were felt enlarged. The septicaemia and pneumonia increased until death on the 12th day. *Post mortem* there were found sloughy ulcers in the rectum, phlebitis and thrombosis of the rectal veins, multiple abscesses in the liver, septic infarcts in the lungs, and *Bacillus aerogenes capsulatus* in the various lesions.

Of all the methods of local anaesthesia, Jonnesco's spinal anaesthesia by minimal doses of stovain with strychnin appears to be at once the safest and surest, and the one to be adopted in combination with small amounts of a general anaesthetic.

Jonnesco (Thoma Ionnescu) of Bucharest, in a pamphlet entitled 'La Rachianesthie Générale', continues the practice he began in 1908. In the course of the following years he advocated his case in France, England, and

America, but failed to gain any following outside of Rumania. He and his colleagues have continued the practice, essentially unaltered. At any rate it forms an interesting series of experiments; he succeeds in producing an analgesia of sensory nerve roots from the fifth nerve downwards. With the minimal doses of stovain combined with strychnin which he uses, analgesia, a loss of painful sensations, is produced, sensations of touch and of heat and cold are retained, also reflexes and voluntary movements are but little, if at all, affected.

Thus even when analgesia of the scalp and face is induced, speech remains unaffected or only slightly blurred. The term 'general' implies that Jonnesco employs his spinal anaesthesia for all cases without the addition of a general anaesthetic or of a narcotic, for all operations from head to foot.

By 1913, the number of operations done in Rumania under his method of spinal anaesthesia amounted to 11,324—1,035 high, i.e. anaesthesia above the level of the umbilicus and 10,289 low.

Jonnesco's own operations numbered 2,436, 505 high and 1,931 low; no death had been due to the procedure and there had been no complications, immediate or late. The practice had been continued during the war.

The essence of the method is the injection into the spinal theca of a minimal dose of stovain mixed just beforehand with a like dose of sulphate of strychnin, the actual dose varying with the height of the injection, and slight modifications are made as the result of experience. For this purpose Jonnesco provides himself with ampoules containing the sterilized drugs, or with solutions sterilized before use.

The ampoules of stovain contain doses varying from 0·5 cgm. to 6 cgm. per 1 c.cm., the ampoules of strychnin sulphate, 1 and 2 mgm. per 1 c.cm. Corresponding solutions are sterilized three times at 100° C. for half an hour each time, at intervals of a day.

Taking a sterilized syringe 1 c.cm. is drawn up from a strychnin ampoule and squirted into the 1 c.cm. contained in the stovain ampoule, which is then warmed over a spirit-lamp to hasten the mixing of the two solutions. Then 1 c.cm. of the mixture of stovain and strychnin is sucked up into the syringe and so forms the injection.

The injection is made with the patient sitting up and bending forward, whenever possible; it is made at one of four places. The **mid-cervical injection** is made midway between the occipital protuberance and the vertebra prominens whilst the chin is bent to the sternum; the needle then enters between the spines of the 3rd and 4th or the 2nd and 3rd cervical vertebrae. The **cervico-dorsal** puncture is made between the 7th cervical and 1st dorsal, or between the 1st and 2nd dorsal spines. The **dorso-lumbar** injection is between the 12th dorsal and 1st lumbar, and the **lumbar** between the 4th and 5th lumbar.

Before making the injection it is absolutely necessary for the cerebrospinal fluid to flow out; in the lower punctures this may occur in a jet, in the higher punctures it escapes by drops. If fluid does not appear, the patient should be asked to cough; if that fails a style is passed down, and this failing, a special syringe is attached and suction made. When after the above, no fluid appears, the needle is withdrawn and another attempt made. A staining of the fluid with blood is of no moment, the fluid should be let drip until it becomes clear. If pure blood escapes, the needle should be withdrawn. The red blood corpuscles have a great affinity for the drugs and rapidly neutralize their action. Fluid must escape before injecting the drugs, which otherwise may be injected outside the dura or even into the cord; moreover, after the injection, it is essential for some cerebrospinal fluid to be drawn back into the syringe. If this cannot be done, it must be assumed that the injection has been a failure. As the injection has not been made into the cerebrospinal fluid, the dose used will not exert a toxic influence, and a second injection into the theca should be forthwith attempted.

As for the amount of the drugs contained in the 1 c.cm. injected, this varies with the height of the injection, the higher the injection the less the amount. Also the dose is modified according to age, state of patient, and presumed length of the operation.

For the cervical and cervico-dorsal injections the dose is 2–5 cgm. of stovain and 0·5–1 mgm. of strychnin; for the dorso-lumbar and lumbar injections, 3–6 cgm. of stovain and 1–2 mgm. of strychnin.

When using the full doses of the above, two injections are made, a combined dorso-lumbar and lumbar injection which may be in equal amounts, a combined cervical and cervico-dorsal injection, $\frac{1}{3}$ in the former position and $\frac{2}{3}$ in the latter.

Children up to 3–4 years of age for operations on the head or neck receive a cervical injection of 0·5 cgm. of stovain and 0·5 mgm. of strychnin; in no case should the dose be more than double, for more than 1 mgm. of strychnin will produce convulsive symptoms. Children over 3–4 support stovain up to 3–4 cgm., but the 1 mgm. of strychnin must not be exceeded.

Old people require, as compared with adults, half the dose of stovain, but the same amount of strychnin. Novocain may be substituted for stovain in doses up to double that of stovain, but with the same quantities of strychnin. However, stovain has proved much more satisfactory.

In order to counteract the fall of blood-pressure, Jonnesco is accustomed, 10–15 minutes before the spinal injection, to give a subcutaneous injection of 25–50 cgm. of caffein. Then, immediately after the spinal injection, the patient is laid flat on the back as the best way of promoting diffusion of the drug and to avoid fainting. When a small dose is injected into the mid-cervical region for a short operation on the head and neck, the head is lowered below the level of the trunk. A longer operation on the head and neck is carried out after combined cervical and cervico-dorsal injections, then the head is not lowered below the trunk.

For operations on the upper extremity and upper part of the thorax, combined cervico-dorsal and dorso-lumbar injections are given, and the body may then be temporarily inclined towards the head. A dorso-lumbar injection will suffice for the lower chest and upper abdomen, if the patient is inclined for a while towards the head.

The immediate results of these spinal injections are divisible into the usual and the exceptional. Among the usual are pallor, sweating, nausea, vomiting, and incontinence of urine and faeces, which occur in some 5–8 per cent.

The exceptional results include a marked fall of blood-pressure, an increased rate and irregularity of the pulse, and an impairment of respiration. Following upon mid-cervical and cervico-dorsal injections, there is a period of transition from normal to an atypical respiration followed by a return to the normal.

'Ce passage ne s'accomplit pas sans une certaine angoisse de la part du malade, et qui peut se transformer en une angoisse plus grande encore pour le chirurgien' (p. 74).

The abdominal respiratory movement begins to diminish in amplitude until after 3–4 minutes it disappears, the movements of the diaphragm having been arrested, as may be confirmed by X-ray examination. Meanwhile thoracic respiration increases in rate and amplitude, including action by the muscles of extraordinary inspiration. After 8–10 minutes the thoracic respiration diminishes, and after 20–25 minutes the breathing returns to the normal, including the diaphragm. Should an overdose, however, be given, the rate and amplitude of thoracic breathing is greatly intensified, then after 2–3 minutes, it becomes superficial and very quiet, cyanosis appears and the thoracic breathing in its turn disappears. If the palpebral and pupillary reflexes are retained, a short recourse to artificial respiration suffices to restart breathing, for then it is not a toxic paralysis of the respiratory centre, but only of all the respiratory nerve roots, which lasts but 2–3 minutes. Jonnesco has never experienced a longer arrest. An excessive dose has had a fatal effect three times in Rumania, in one case after a mid-cervical injection of 4 cgm. of stovain, in a second after 2·5 cgm. of stovain, in a third after 4 mgm. of strychnin.

After the mid-cervical injection of a minimal dose, analgesia commences in the frontal and temporal regions and then descends to the face, neck, and upper chest as far as the nipples. Meanwhile the palpebral and pupillary reflexes are retained, also the pharyngeal and laryngeal reflexes, which latter are of such importance in the case of operations on the mouth and throat. The motion of the face and lips is retained, the patient can spit out from the throat at will, although speech may be for a time a little impaired. After the cervico-dorsal injection the analgesia first appears on the front and sides of the neck, and with the patient lying flat on the back, it ascends to the level of the hairy scalp; it includes the upper limbs and descends to the level of the xiphoid cartilage. There may be a slight impairment of muscular force and of reflexes in the upper limbs, but the voluntary movements of the upper limbs are on the whole preserved and a complete paralysis almost never occurs. The anaesthetic affects chiefly the posterior roots and, in the minimal dose, the anterior roots hardly at all. Consciousness is completely preserved, the eyes are screened off, and the patient is engaged in conversation, the ears not being plugged.

Huff, who paid a visit to the Eforia Civil Hospital at Bucharest, watched the removal of a lipoma from the shoulder after a mid-cervical injection. The man discussed the operation during its entire progress; the conversation was not directed to distract the patient's attention. (The doses in Huff's report are confused by errors in printing the figures.)

Jonnesco quotes two instances in favour of the patient remaining conscious; to the surgeon accustomed to operate under general anaesthesia, the two examples will point to a conclusion directly the opposite. In one case Jonnesco, after exploring an injured arm, found it necessary to amputate, and thereupon asked the patient's consent, the possibility of a necessity for amputation not having been mentioned to the patient or his friends beforehand. From another patient Jonnesco had just removed the gall-bladder in accordance with the previous indications and diagnosis, thereupon the patient demanded that before his abdomen was closed, all the rest of his abdominal viscera should be examined. This was done and no further disease was found, indeed there had been previously no other indications of disease except in connexion with the gall-bladder.

No patient during the course of 11 years had refused Jonnesco's proposal, and he has never been forced to have recourse to anaesthesia by inhalation.

As to the after effects, headache has only been marked in 6 per cent., the severest have occurred when blood has mixed with the fluid or slight leucocytosis has been set up. As there is no increase of tension lumbar puncture only makes the headache worse. Spinal pain is much rarer than headache.

Nausea and vomiting do not occur after the analgesia has passed off. Incontinence of urine and faeces is transient and only occurs after the same operations in which it also occurs when the anaesthetic is administered by inhalation. Paralyses were absent except in 3 cases in which there was paralysis of the external rectus, in one case for 6 months, in the other two for only a couple of weeks. Jonnesco suggests that there was a predisposing factor, e. g. latent syphilis. In only 1 per cent. was there an unexplained rise of temperature, and then only to 39·6° C., and a return to normal in 24 hours, the cerebrospinal fluid remaining normal.

Among the advantages claimed were the following: in operation on the brain there is less tendency to hernia cerebri; in operation on the face, mouth, and throat the patient can spit out blood and mucus at will and protect his larynx; abdominal movement is almost absent and is not variable; in abdomino-pelvic operations the intestines are easily kept back; in operations on the bladder both the abdominal wall and the wall of the bladder are relaxed; the limbs being completely relaxed, the reduction of fractures and dislocations and the breaking down of adhesions are rendered easier; in difficult labour needing manual interference, a suitable dose removes pain and promotes relaxation, whilst the contractility of the uterus is not impaired.

The routine use of spinal anaesthesia by stovain to produce anaesthesia below the level of the umbilicus was favourably reported upon by Weston. He operated in Lucknow, mostly on British soldiers. Of 170 cases no higher segments were involved than were necessary for appendicectomy. Headache after the operation was avoided by moving the patient to his bed without shaking, and the headaches which occurred were relieved by phenacetin and caffein. Prospective patients on hearing from their comrades preferred spinal to general anaesthesia. Barker's stovain glucose solution was used.

Boyd and Yount, also in a hot climate, at Panama, reported favourably on the results in 6,229 cases for operations below the umbilicus. The injections were made by 27 different medical men on West Indian negroes and poor natives of Panama. The most constant results occurred with stovain in salt solution; for short operations the dose was 5 cgm., the average 7 cgm., and the maximum 8·5 cgm. They rejected the procedure for neurotic patients, patients with spinal disease or deformity, or those with septic infection near the site of puncture. No complications followed immediately upon the injection except when the fluid was allowed to spread to higher segments by lowering the head to the Trendelenburg position. Three men required artificial respiration, one of these for fifty minutes.

After the operation moderate headache occurred in 20 per cent., severe headache and vertigo in 1 per cent., attributable to a serous meningitis. Three had pains in the legs from puncture of nerves of the cauda equina.

There was also temporary incontinence; vesical incontinence might last two weeks.

In 4 cases the method appeared to be the cause of the death. One apparently quite healthy man died instantly upon the puncture. The puncture having been made and fluid not appearing, a second case was asked to cough, and upon doing so he at once collapsed and ceased to breathe; he could not be resuscitated; no stovain had been injected; there was no post-mortem examination. In a third case the woman's blood-pressure was lowered by the spinal injection: during the manipulation of an ovarian cyst, it burst, whereupon the woman collapsed and died in a few minutes upon the operating table. A woman, for whom Caesarean section was intended to relieve eclampsia, had high blood-pressure which was lowered a little by the stovain injection. Shortly after this, and before the commencement of the operation, there was a violent convulsion, she became cyanosed and ceased to breathe. The convulsion may have been essentially a fatal one; there was no post-mortem examination.

Rood, from a large experience of 8,000 cases of spinal anaesthesia with stovain by A. G. Barker's methods, confirmed the importance of combining spinal and general anaesthesia. Shock is reduced in long surgical operations, such as those for the removal of malignant disease of the uterus or rectum, in the case of excisions and amputations at the hip-joint in children, and for relaxation of the abdominal wall in the presence of chest complications. But spinal anaesthesia was contra-indicated if there was already shock, also if there was heart disease, especially aortic, for it then tended to cause a dangerous fall of blood-pressure. As for common operations in healthy men for hernia or varicose veins, and appendicectomy, the adoption of low spinal anaesthesia afforded experience which would be of service in cases in which the method was definitely indicated.

Achard gave his experience of accidents and failures among 400 cases of spinal anaesthesia. In all this was limited to below the umbilicus, in some three-fourths novocain and in one-fourth stovain was used. No deaths occurred and no lasting paralyses. Nausea, vomiting, and syncope were avoided by keeping the patient quiet mentally and bodily, and by not moving him into an abnormal position, Trendelenburg or prone, until the anaesthesia was well established. Morphia beforehand merely stupefies; it does not prevent nausea and vomiting, but combined with strychnin may counter a tendency to faint. Incontinence may be troublesome, especially in certain operations, unless there has been complete evacuation beforehand. Towards the end of the anaesthesia tremor and headache may set in. After the operation, the chief trouble was the headache, also heaviness in the loins, 'courbature', more rarely spinal pain and abdominal discomfort, 'état suburral', until relieved by a purge. As to failure, complete failure was chiefly ascribed to lack of experience; partial failures were due to the anaesthesia being insufficiently intense or lasting, especially when it had been neutralized by stimulants required owing to syncope. The anaesthesia might be partial, its spread within the theca being limited to the posterior root segments corresponding to the level of the injection, or be only unilateral when the patient had been injected whilst lying on his side. Immediately following the injection the patient should be laid on the back for 10 minutes.

The Germans, during the war, have chiefly used tropacocain, but with the addition of adrenalin, for producing anaesthesia below the nipple. There have been variable reports, fatal cases and grave complications on the one hand, or only the usual sequelae. There seems to have been differences in the quality of the tropacocain used, and the addition of variable proportions of adrenalin prevent any exact opinion as to dose. Further, there is uncertainty whether the arrest of breathing was due to the drug being allowed to spread up too high, e.g. by placing the patient in the Trendelenburg position (see Brunn, Flörcken, Kirschner, Zeigner, and Calman). Jonnesco's method is the only one which has been shown to be safe, all the others are entirely dangerous at levels above the umbilicus. Both heart and respiration may be simultaneously affected and life only saved by the heroic measures adopted in Cooper's case. A woman, apparently healthy, had nearly died some years before under a general anaesthetic given for curetting the uterus. Appendicectomy being necessary, stovain was injected and the pelvis raised. Numbness soon spread to the fingers, she became very pale, whispered unintelligibly, and the breathing became imperceptible. In spite of artificial respiration and stimulants, the pulse also became imperceptible. The heart was then massaged through the diaphragm, whilst Sylvester's artificial respiration and Laborde's rhythmic traction on the tongue were kept going. An occasional respiration ensued, but the resuscitation had to be continued for three-quarters of an hour. Appendicectomy was then carried out; the patient regained consciousness and called loudly for air. Oxygen was administered for some hours; there were no further complications and recovery followed.

In order to avoid the dangers incident to the employment of full doses for intraspinal injection the sensory nerve roots have been injected alongside the vertebrae, also in the brachial, splanchnic, and pelvic plexus. A commencement was made by Selheim in 1905 in order to perform ovariotomy. Larger doses are used combined with adrenalin than in spinal injections, but the paravertebral injections necessitate the making of multiple punctures on both sides, and as the point is directed to the nerves, it is likely that severe pain is caused. This adds further complexity to the method because it has suggested the induction of preliminary somnolence by means of scopolamin and morphin.

Among the instances of the dangers attending paravertebral anaesthesia, Pauchet described the injection of the five or six nerves supplying the abdominal wall and viscera on each side. In a case in which 10 injections, 5 on each side were made, 5 cgm. of cocain were administered in each injection and death followed. In another case 70 cgm. altogether of cocain were injected. Cyanosis, with spasm of the respiratory muscles, ensued for 40 minutes. Pauchet himself advised novocain, even then fainting occurred, especially when the dorsal nerves were injected. With all the minute directions as to the insertion of the needle alongside the body of the vertebra, the actual distribution of each injection must be variable.

Wiemann noted two fatal cases following paravertebral injections in the cervical region, preliminary to operating for bronchocele.

In his own case, a woman aged 29 had a generally enlarged bronchocele attended by dyspnoea, headaches, and a pulse-rate varying between 88 and 114. Some narrowing of the trachea was shown by X-rays. The heart and other organs were sound as confirmed *post mortem*. After a preliminary injection of 1 cgm. of morphin, 7 c.cm. of a 1 per cent. novocain and suprarenin solution was injected on each side between the 3rd and 4th cervical vertebrae, and then 20 c.cm. of a 0·5 per cent. of the novocain-suprarenin solution was injected under the line of the incisions through the skin. (Total novocain injected 0·38 grm. Total suprarenin 0·00076 grm.) As the local anaesthesia was becoming established, the respiration and heart simultaneously failed and could not be restarted. There was found an extravasation of blood on either side of the vertebrae, apparently from puncture of the vertebral arteries; the extravasation had infiltrated the vagi nerves and the sympathetic ganglia.

In a case under Brutt a woman aged 29 had a recurrence of a goitre with dyspnoea but no other complications. After a preliminary scopolamin and morphin injection, the line of the incision was injected subcutaneously and then the bilateral paravertebral injection made. Altogether 140 c.cm. of a 0·5 per cent. novocain and suprarenin solution were used. Five minutes after the establishment of complete anaesthesia of the skin the respiration and heart ceased simultaneously, all attempts at resuscitation failed. Nothing was found *post mortem* to account for the death.

Kappis practised an injection of the splanchnic nerves and plexuses. From the 1st to the 3rd lumbar nerves, sensory fibres may be traced through the rami communicantes lumbales and the splanchnics to the retroperitoneal ganglia. Sensory fibres are thence distributed to the mesentery, to the gastrohepatic and gastrocolic omentums, common bile and cystic ducts, the hila of the kidneys, and the region of large blood-vessels. The injection was made in 200 cases under the 12th rib, 7 cm. from the line of the spinous processes. The needle is entered horizontally, but is directed inwards at an angle of about 30° until the point of the needle is touching the side of the body of the vertebra, then the point is directed forwards. Thereupon 20–40 c.cm. of 1 per cent. novocain-suprarenin solution is injected, also 10–20 c.cm. by passing in the needle between the 1st and 2nd lumbar transverse processes. Naegeli injected the sensory fibres of the viscera in the same way. Operations were then carried out on the stomach, liver, gall-bladder, duodenum, small intestines, colon, spleen, and kidneys. The sensory nerves of the stomach are connected with the 6th–10th dorsal, those of the caecum with the 11th dorsal to 1st lumbar, the sigmoid with the 3rd lumbar roots. The fibres run through the greater and lesser splanchnic nerves. Below the 3rd lumbar the afferent course is from the rectum and urogenital apparatus to the hypogastric plexus. About the 6th dorsal no sensory fibres reach the cord from the abdomen. The vagus takes no part in conducting painful sensations; neither do the sympathetic lateral chains.

Kulenkampf in 1911 commenced the practice of injecting the brachial plexus in order to anaesthetize the upper extremity. Complications have been of two kinds, after the operation a temporary paralysis has followed with slow recovery, or partial but permanent nerve degeneration. In some of them a tourniquet had been used, in some not. Besides this the injection has been wrongly made, either into the dome of the pleura or into the anterior mediastinum. Flesch-Thebesius noted one case in which a prolonged paralysis of the ulnar, median, and musculospiral nerves ended in incomplete recovery, some nerve and muscle degeneration having been set up. An Esmarch's band had been applied to the arm whilst the median nerve was being freed from the scar occasioned by the wrist being cut by broken glass. The operation lasted 40 minutes. But he quotes cases in which no band had been used.

Mulley quoted cases in which pleurisy and pneumothorax was set up. In a man aged 16 anaesthetized to reduce a dislocated elbow, severe pain on that side followed immediately upon the injection, stabbing pain and dyspnoea continued, and he suffered from serous pleurisy for a long while. In another case, also of a dislocated elbow, the pain set up by the injection was so severe that the reduction had to be postponed. In two cases a pneumothorax was caused. In another case, in addition to the pneumothorax, there was surgical emphysema and it became necessary to drain the pleura. In one case both the dome of the pleura and the apex of the lung were involved with extravasation of blood. There was a rapid swelling of the supraclavicular region, the swelling being a pale blue and crackling when palpated. Emphysema and impairment of breathing progressed until death two days after the injection. There was found pneumothorax with complete collapse of the lung, which was otherwise healthy. The danger to the dome of the pleura is the more probable when the point of the needle touches the inner cord immediately above the third part of the subclavian artery and causes a sensation in the little finger. Mulley tried injection higher up, three fingers' breadth above the clavicle and just behind the external jugular vein. At this spot, the injection is likely to infiltrate the phrenic nerve and there will then occur arrest of that half of the diaphragm. This paralysis begins to pass off after four hours, and in 24 hours the movements of the diaphragm may be again normal. At any rate the injection must not be made on both sides at once.

Weil noted the remarkable result of injecting fluid and air into the anterior mediastinum, in front of the pericardium, which produced the same effect as the experiments of Reynier made in 1880. Immediately upon the injection there occurred a feeling of oppression over the heart, and of want of air. A collection of air and fluid between the sternum, pericardium, and pleura produced with each beat of the heart a noise like that of a water-wheel, (bruit de moulin. Mühlengeräusch). The next day a loud double noise could be heard at 1–2 m. from the patient, synchronous with the heart-beat, mainly systolic, making a metallic clucking or slapping sound. This was independent of breathing; there was no emphysema, even in the neck. The noise disappeared in four days.

On the whole, and in spite of the many successful cases reported, it would appear that Kuhlenkampf's procedure is both uncertain and unsafe.

Parasacral injection anaesthesia as used by Casper when operating on the prostate has been already mentioned in a previous number (*Medical Science*, 1920, **1**, 424). An epidural sacral injection was described by Fischer as a means of obtaining sufficient anaesthesia for all operations below the diaphragm. His method may be briefly described, if only to be rejected. The patient having been rendered somnolent by veronal and morphin begun overnight, is laid prone with the head and trunk horizontal and the legs hanging over the end of the table at an angle of 45° degrees with the trunk. Then the needle is inserted through the posterior sacrococcygeal membrane, into the spinal canal. It is then pushed on for 5–7 cm. by feeling the way with the point against the bone, so as not to penetrate the lower end of the theca. Neither cerebrospinal fluid nor blood should return through the needle on withdrawing the mandrin. Should fluid appear, the point of the needle is withdrawn a little and then pushed on again. The needle being inserted, before the injection is made the patient's head and trunk are lowered, so as to hang down at least 45° below the horizontal. The injection consists of novocain 1·5 per cent. with the addition of a drop of suprarenin to every 10 c.cm. The amount injected was 70 c.cm. for operations on the upper abdomen and lower limbs; for cachectic patients it may be reduced to 50 c.cm., for children under 15 to 40 to 30 c.cm., the latter was the dose used for a weakly girl of 13.

The upper limit of anaesthesia so produced was in about half the cases between the 2nd rib and nipple.

Fischer had experienced only one fatal case. A woman exhausted by gastric ulceration and suffering from perforation of the ulcer was injected with 63 c.cm. of the novocain-suprarenin solution and died in 20 minutes without the operation having been begun. In other hands the method had been followed by deaths, epileptiform seizures, retro-gluteal phlegmon, and a number of the other complications already referred to.

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ABSTRACTS

SURGERY

Neander, A. Något om radikaloperation av bröstkräfta. [**Results of operations for cancer of the breast.**] *Hygiea*, 1919, **81**, 937–52.

This paper is a review of the experience gained in the surgical wards of the Serafimerlasarette, Stockholm, in the period 1890–1914, during which 439 cases of cancer of the breast were operated on. Of these, 427 underwent radical operations, i. e. the field of operation included the axilla as well as the breast itself. The immediate operation mortality was 2·1 per cent. (nine cases). A study of these operation fatalities in detail showed that, provided the patient's health is sound before operation, the risk of an 'operative death' is negligible. In his analysis of the results Neander excludes the cases in which the disease was found to have spread beyond the axilla and past the clavicle, for in such cases the operation was not radical in the sense that all the demonstrably diseased tissues were removed. By this process of exclusion, the 418 patients surviving the operation were reduced to 321. Of the 97 cases thus excluded from further analysis, 77 had died of cancer, 5 of other diseases, and 15 could not be traced. Of the 321 patients on whom an apparently radical operation had been carried out, 165 had died of cancer, 23 of other diseases without any sign of a local recurrence of the cancer, 45 were still alive and well, 85 could not be traced, and 3 were alive, but suffering from a recurrence of the disease. If an observation period of at least five years be accepted as the test of the effect of a radical operation, then the results for 284 patients operated on in the period 1890–1912 were: fatal recurrence of the disease, 145; deaths from other causes, 23; still alive and well, 34; alive, but suffering from a recurrence of the disease, 1; not traced, 81. Of 165 cases of recurrence 137 proved fatal within three years of the operation, and 21 between the third and fifth year. Only 7 had developed recurrence of the cancer more than five years after operation.

In another series of investigations Neander shows that, after the age of 30, three-quarters of all cases of chronic disease of the breasts are malignant. During the past five years 65,000 patients were registered in the polyclinic of the Serafimerlasarette, and of these 173 suffered from chronic disease of the breasts. Of these, again, 123 were over 30. In 94 of these cases the disease was cancer, and in 1 it was sarcoma. Thus the proportion of malignant cases to the total was 72 per cent. Neander justifies his pessimism as to the prognosis for cancer of the breast by showing that about 25 per cent. of all cases are inoperable, and that more than 70 per cent. of the cases undergoing a radical operation terminate fatally in less than three years with a recurrence of the disease. Neander has adopted

Steinthal's classification, and has found that 71 of his cases belonged to Class I (small, slowly-growing tumour of the breast, with little or no enlargement of the glands in the axilla). Of these, 32 had died of cancer of the breast, 3 of cancer of the stomach, 6 of diseases other than cancer, and 30 were still alive and well. In Class II (comparatively rapid growth of the tumour, with fixation to the skin and definite enlargement of the glands in the axilla) there were 151 patients, 125 of whom had subsequently died of cancer of the breast. Three had died of cancer elsewhere in the body, 10 had died of other diseases, and 13 were alive and well. All the 15 patients in Class III (with involvement of the supraclavicular glands) had died of cancer, although these glands had been removed.

Discussing the causes of recurrence, Neander notes that in 82 cases the disease broke out again in or near the scar of the operation wound. In 31 cases the recurrence was first noted in the glands of the axilla, and in 22 cases in the supraclavicular glands. The fact that in about two-thirds of all cases of recurrence the disease appears in or near the operation scar indicates the necessity for a more sweeping removal of the skin than heretofore. Neander suggests that surgeons have hitherto been too obsessed by the ambition to achieve healing by first intention; the skin should be removed over a wide area, even at the cost of early, primary union. Another point to which he attaches considerable importance is the exploratory operation in doubtful cases. It may be a confession of the surgeon's inability to diagnose every case off-hand, and some surgeons scoff at the timid ignorance betrayed by exploratory punctures and operations. But they are often necessary if the patient is to be spared much needless pain and distress.

C. L.

Teilmann, F. Luxatio habitualis capituli fibulae. [**Obscure symptoms due to recurrent dislocation of the head of the fibula.**] *Ugesk. f. Læger.*, 1920, **82**, 110–11.

Discussing the difficulties of diagnosis of recurrent dislocation of the head of the fibula, Teilmann reports the case of a woman, aged 25, who felt sudden pain in the right knee as she straightened herself up after buttoning her shoes. During the following night the pain became worse, radiating from the knee both up and down. She was totally incapacitated and was confined to her bed, being treated with compresses and salicylates without benefit. No fluid could be found in the joint, which was tender. When the head of the fibula was pressed from behind and below, it slipped forward, provoking an attack of pain which radiated in the manner described. When the pressure was released the head of the fibula sprang back into place. The leg could be over-extended at the knee, in which position the fibula was dislocated forward. She was discharged from hospital with a plaster-of-Paris splint, the wearing of which prevented the dislocation. But it recurred soon after she dispensed with the splint. Arthrodesis was accordingly performed. No fluid escaped from the superior tibio-fibular joint when opened. It was normal apart from the laxity of its capsule, and it did not communicate with the knee-joint. The articular surfaces were removed, and a screw was driven through the head of the fibula into the tibia. Complete recovery was effected. Teilmann observes that the surgeon is apt to overlook this condition unless he bears it in mind or is lucky enough, while examining the knee, to displace the head of the fibula.

After the operation the leg could not be over-extended at the knee, and it is possible that its abnormal range of movement before the operation was connected with the dislocation. C. L.

Fog, R. M. Et ejendommeligt Tilfælde af recidiverende Myositis. [**Micrococcus crassus myositis.**] *Hosp.-Tid.*, 1919, **62**, 1402–5.

Fog gives details of a case, no parallel to which he can find in the literature. His patient was a boy, aged 15, who had shown no sign of rheumatic fever, but who had suffered from measles, rubeola, and two attacks of parotitis. A blow on the left shin at the age of 10 did not break the skin, but rendered the leg so painful that he had to go to bed a day later. The limb was slightly swollen, but there was apparently no fever. During the next five years this pain and swelling recurred every spring without any apparent provocation. Each attack lasted two or three months, during which the patient was kept in bed and treated as for rheumatic myositis. In March 1919 he was admitted to hospital with considerable swelling from the middle of the left thigh to a point a little below the knee. The overlying skin was slightly reddened. The outer aspect of the thigh was very tender, and the tissues were infiltrated, but there was no fluctuation. There was a considerable effusion into the knee-joint, but the leg was not painful when jarred, and the inguinal glands were not enlarged. The diagnosis of osteomyelitis would have been inevitable but for the comparatively low temperature and a negative X-ray examination. When the outer aspect of the thigh was incised and the fascia divided, very oedematous, pale and jelly-like muscle bulged forward, and some fluid escaped under slight pressure. No abscess could be found, and the periosteum of the femur seemed healthy. A bacteriological examination of the muscle and fluid revealed the *Micrococcus crassus* in pure culture. This was also found in the nose. An autogenous vaccine was given, and the patient discharged cured. Fog is doubtful as to the ability of this vaccine treatment to prevent a recurrence of the disease in the spring of 1920. C. L.

Rietz, T. Om narkostremor och dess hävande. [**Control of the tremor of general anaesthesia.**] *Hygiea*, 1919, **81**, 330–6.

Rietz notes that in no work on surgery or general anaesthesia has he been able to find a word about the tremor occasionally observed during anaesthesia. Yet this complication is a serious inconvenience to the surgeon. It usually affects the lower limbs, but the lower half of the trunk may also be involved. The muscular, rhythmic contractions follow each other in quick succession, and are sometimes so pronounced as to assume the proportions of clonic convulsions. At other times this condition is so abortive that it is limited to a few twitchings lasting only ten seconds. In two cases the tremor lasted over five minutes, interfering greatly with the operation.

Between 1912 and 1919 Rietz has observed 28 such cases, the proportion of males to females being 27 to 1. The age distribution was fairly uniform between 16 and 68, but this condition was never seen in persons under 16. Investigations as to predisposing factors, such as epilepsy, alcoholism, a nervous temperament, &c., proved negative. Nor were these cases distinguished by great restlessness during the early phases of anaesthesia. The duration of anaesthesia, and the amount of the anaesthetic administered, also appeared to exercise no influence on the incidence and degree of the tremor. The anaesthetic was pure ether in 26 cases, and a mixture of ether and chloroform in 2 cases. There was no reason for assuming that impurities of the anaesthetics were responsible for the tremor, as only a proportion of the patients anaesthetized from the same bottle reacted in this manner. No relation could be established between the incidence of the tremor and the site of the operation. Thus the only positive finding of significance was the great disparity in the sex incidence. In about half the number of cases the stage of anaesthesia at which tremor occurred was noted. It occurred at the beginning of anaesthesia in 3 cases, at the beginning and in the middle of anaesthesia in 2 cases, in the middle in 1 case, in the middle and towards the end in 1 case, towards the end in 6 cases, and throughout anaesthesia in 1 case.

The whole character and course of this condition resembled so closely other forms of tremor commonly associated with stimulation of the motor tracts and cortex, that it seemed probable that the anaesthetic circulated by the blood stimulated the brain of susceptible persons. On this assumption checking the supply of drugged blood to the brain should reduce the tremor. Working on this hypothesis, Rietz exerted powerful pressure for a few seconds in the carotid fossa of a boy of 16, whose tremor ceased instantly. It recurred when the pressure was relieved, ceasing again at once when it was renewed. When it was maintained for about 15 seconds, the tremor ceased for good. Subsequent observations showed that the response of the tremor to this device could be graduated; if the pressure was slight, the tremor was only partially arrested. This device was practised in 25 of the 28 cases. It was entirely successful in 16 cases, partially successful in 4, and a failure in 5. The degree of success probably depended to a certain extent on variations in the blood-supply to the brain in different persons. The efficacy of this device did not seem to depend on the degree of the anaesthesia nor on the stage it had reached. But though the technique is simple, some dexterity is required if the compression is to be effective. To assure strong enough compression the anaesthetist should not sit behind the patient's head, but should stand beside him, his head being turned away from the anaesthetist, who exerts pressure either with his thumb or with four fingers of the same hand.

Anticipating the suggestion that his achievements might be due, not to compression of arteries but to a painful reflex, Rietz has attempted to control this tremor by conveying painful stimuli to the brain by such means as powerful pressure exerted on the nerve-trunks in the axilla. None of these devices had any effect on the tremor. He concludes with the reassurance that this method of controlling the tremor of anaesthesia entails no discomforts or dangers.

C. L.

Saugman, C. Erfaringer fra Vejlefjord Sanatorium om Thoracoplastik ved Lungetuberkulose. [**Extrapleural thoracoplasty in pulmonary tuberculosis.**] *Ugesk. f. Læger*, 1919, **81**, 585–609.

Professor Saugman had treated up to the end of December 1918 26 cases of pulmonary tuberculosis in the third stage of the disease with thoracoplasty. Excluding the 6 cases still under treatment at his sanatorium, he shows that of the remainder 10 were rendered capable of light or heavy work, 4 were improved, and 6 had terminated fatally, 2 within a couple of days of the operation. He is greatly impressed by the successes which can be achieved by this operation in otherwise perfectly hopeless cases. C. L.

NEUROLOGY

Mendel, K. Familiäre peripherische Radialislähmung. [**Familial musculospiral paralysis.**] *Neurol. Centralbl.*, 1920, **39**, 58.

Charcot, Oppenheim, and several other observers have recorded small series of cases of familial facial palsy, though whether this depended upon a congenital smallness of the fallopian canal, or an inherent vulnerability of the nerve has never been determined. Mendel has been unable to find any reported cases of familial musculospiral paralysis, and he now describes a series of three cases in a father and two sons. One of these came under observation. The patient was a boy of 14 years, in whom for no discoverable cause a sudden paralysis of the right musculospiral nerve developed.

Twenty years earlier the father, a cigarette-maker, had also suddenly developed a left wrist-drop which took six months to clear up completely.

A brother of the patient also gave a history that after carrying a load on one shoulder, one hand had suddenly become weak and numb on the dorsal surface.

Both the father and the present patient had the habit of leaning their heads on their hands with their elbows on the table, and it was after sleeping in this position after dinner that the paralysis had appeared in the case of the former. There was no hereditary history of similar complaints.

Mendel is of opinion that an inherent susceptibility of the nerve was responsible for the condition in these cases. F. M. R. W.

Hala, W. and **Smith, C. M.** **A case of meningo-encephalitis (lethargic encephalitis).** *Arch. Neurol. and Psychiat.*, 1920, **3**, 160.

Clinically the case was diagnosed as lethargic encephalitis. There were lethargy, paralysis in the distribution of the third, sixth, seventh, tenth, and twelfth cranial nerves, rigidity of the muscles, a mask-like face, and an absence of signs of involvement of the pyramidal tracts. Pathologically, the authors found septic meningo-encephalitis and ependymitis, with punctate haemorrhages and perivascular infiltration of the centrum ovale, and basal ganglia. There was a large subdural clot over the right fronto-parietal cortex.

Just before death they found in the cerebrospinal fluid, and after death in the purulent meningeal exudate, a Gram-negative motile bacillus probably belonging to the colon-typhoid-enteritidis group. They regard this as the causative organism. F. M. R. W.

Kahn, E. (1). Psychopathen als revolutionäre Führer. [**Psychopaths as revolutionary leaders.**] *Ztschr. f. d. ges. Neurol. u. Psychiat.* (Orig.), 1919, **52**.

Kahn, E. (2). Psychopathologie und Revolution. [**Revolution and psychopathology.**] *München. med. Wchnschr.*, 1920, **67**.

In these two papers, Kahn deals with the reaction of psychopaths to the early war conditions and to the later revolutionary upheavals in

Bavaria. In the early days they were among the most exalted and enthusiastic of volunteers for the front, while at the other extreme the most determined opponents of the war were likewise recruited from their ranks.

The inspirers and leaders of the revolution during the terminal phases of the war were also pyschopaths, and these he divides into four types: those who are ethically defective, hysterics, fanatical psychopaths, and individuals of manic-depressive tendency. Fifteen examples of these types are described and their histories given. Among them is included, under a false name, a prominent legal official. In the first group, vanity and avarice were the motives determining conduct, while in the case of the hysterics their uncontrollable impulses carried them on. Individuals of the fanatic type, with all their altruistic zeal, desired most of all to stand in the limelight, while those of the fourth type hastened delightedly to avail themselves of the opportunity to attract attention to themselves.

In every instance, egotism, a tendency to exaggeration, and a dictatorial frame of mind were very manifest. This and much more of the kind Kahn lays to their charge, and he concludes that, in spite of many gifts which the revolutionaries displayed, their want of common sense and of judgement, their inability to co-operate with others, and their lack of character vitiated all their proceedings.

He remarks how, in every social upheaval, these abnormal and disagreeable individuals, who cannot get on with their fellow men, are always eager to throw in their lot with the forces of unrest, thus to get their own back on society. F. M. R. W.

Rompe. Polyneuritis und Meningitis nach Mumps. [**Polyneuritis and meningitis after mumps.**] *Monatschr. f. Kinderh.*, 1919, **15.** (*Ztschr. f. d. ges. Neurol. u. Psychiat.* (Ref.), 1920, **20**, 25.)

The nervous complications of epidemic parotitis may take the form of a meningitis, an encephalitis, or a neuritis. The meningitis when it occurs is serous and of good prognosis. Encephalitis is a complication of convalescence and results from infective embolism, and abnormalities of the pupils and paralytic phenomena are the rule. The prognosis is but moderately good, and residual symptoms may be left in severe non-fatal cases. Neuritis is an earlier complication and may be seen as early as the second week. It is a polyneuritis with involvement of the facial and auditory nerves, and, except as regards recovery from the cranial nerve affection, prognosis is good.

Rompe describes a case which he considers as one with polyneuritis and meningitis. F. M. R. W.

Herrmann, E. Apoplexie und Hypertonie. [**Cerebral haemorrhage and hypertension.**] *Neurol. Centralbl.*, 1920, **39**, 82.

The author quotes Strasser (1919) as finding that, of all cases of high tension, only those in which there are definite signs of arteriosclerosis or chronic nephritis are prone to cerebral haemorrhage, while the type known to English authors as 'capillary fibrosis' shows no special liability to this condition. Thus, of 95 arteriosclerotics with high blood-pressure 8 had cerebral haemorrhage; in 29 cases of nephritis there were 6 cases of severe apoplexy; while of 34 cases of simple hypertension ('einfacher Hypertonie') none showed a cerebral lesion.

Herrmann has approached the problem from the opposite point of view and has endeavoured to determine the relation of these forms of hypertension to a series of cases of cerebral haemorrhage. He has observed 44 cases, half males and half females. Their ages ranged from 50 to 90 years, and their respective blood-pressures from 140 to 270 mm. of mercury. Of these no less than 35 showed definite signs of arteriosclerosis; rigid arteries, headache, giddiness, intermittent claudication, and so on. Four had chronic renal lesions, and two were old syphilitics with positive Wassermann reactions.

Details of the progress of the cases are given, and Herrmann concludes with Strasser that 'essential' hypertension does not lead to cerebral haemorrhage, but unfortunately the differentiation of this particular form is apt to be extremely difficult, and hence the practical value of these two sets of observations is largely lost. F. M. R. W.

Meissner, R. Medianuslähmung mit folgender Phrenicuslähmung nach Schussverletzung. [**Gunshot wound of the median nerve followed by paralysis of the phrenic.**] *Neurol. Centralbl.*, 1920, **39**, 84.

From a gunshot wound of the middle third of the left upper arm, a painful lesion of the median nerve resulted with the usual motor, sensory, and trophic changes.

About three months later there developed acute pain in the chest and epigastrium. Respiration was painful, and after food the abdominal pain was severe and of a persistent stabbing character. Later pain appeared posteriorly in the chest. Yawning and deep breathing aggravated the chest pain. There was no cough and no vomiting. Radiographic examination revealed complete paralysis of the left half of the diaphragm.

Treatment with radiant heat, diaphoresis, and drugs such as aspirin resulted in complete recovery of the phrenic lesion in four weeks.

In explanation of this sequence Herrmann suggests that, since the fifth cervical root may be common to both the median and the phrenic nerves, there may have been an ascending neuritis of the former which, extending to this common root, produced a neuritis of the phrenic.

It may be doubted, however, whether the author has established this. There seems to have been a moderate grade of causalgia in association with the median nerve lesion, but this is scarcely enough to support the view of an inflammatory ascending neuritis reaching the spinal roots, even if this were a condition in which we had any sound reason to believe. It appears from the case record that the lesion of the phrenic was in all probability a neuritis, but of its aetiology there are no data upon which to form an opinion. F. M. R. W.

Holker, J. A method of testing the temperature sense. *J. Path. and Bacteriol.*, 1920, **23**, 188.

An apparatus for testing temperature sensation is described. For this it is claimed that the temperature of stimulation can be kept constant and varied at will. The area of stimulation is also constant and capable of modification as desired.

It consists of a glass tube 10 cm. long by 3 cm. wide. The bottom is closed by an extremely thin cone of phosphor bronze, with a slope of 45° and a flat apex. A rubber stopper with a thermometer inserted through it closes the top. The desired temperature can be obtained by an appropriate freezing mixture, for which several formulae are given.

For temperatures above that of the atmosphere the vessel is partly filled with water electrically heated by a resistance wire, the temperature being standardized by a mercury thermo-regulator. The paper contains the complete technical details of construction.

In a footnote, Dr. Stopford refers briefly to his experiences of sensory testing with this apparatus. F. M. R. W.

Strümpell, A. Die myostatische Innervation und ihre Störungen. [**Myostatic innervation and its disorders.**] *Neurol. Centralbl.*, 1920, **39**, 2.

In this paper Strümpell states, in a general fashion, views that have already been criticized in these pages (vide *Medical Science*, 1919, **1**, 209). He says that since the elucidation of the origin and course of the pyramidal system of fibres there has been a tendency to attribute all disorders of motion to lesions of this system, with the possible exception that the equilibration of the body has been associated with the activity of the cerebellar system. He lays stress on the relative smallness of the pyramidal tract as seen in cross sections of the cord, when contrasted with the importance of the functions ascribed to it.

He develops his thesis of the motor innervation of the skeletal muscles as follows: most of our skilled purposive movements, especially skilled occupation movements of the hands, employ relatively few muscles, but if they are to be properly carried out they demand a widespread synergic fixation of other muscles in the arm, and indeed in all the body musculature. For example, the painter standing at his easel performs the skilled movements peculiar to his occupation with the hand and wrist, but the arm must be maintained in a suitable posture before this is possible, while, in addition, his whole attitude must be adapted to facilitate the work of the small active portion of his musculature. This widespread synergic action is practically subconscious, and is so finely co-ordinated a process that, so Strümpell argues, its nervous mechanism must be highly specialized. Therefore he divides the innervation of the musculature into a 'myodynamic' factor governing the voluntary skilled movements, and a 'myostatic' factor regulating the static and fixating functions.

This is a very interesting hypothesis, and may be new and unfamiliar to German neurologists, but in this country the work of Hughlings Jackson, of Beevor, and of Sherrington long ago lifted this subject out of the realm of pure speculation. In the last century Jackson drew attention to the dual aspect of motor innervation. He showed that there was a 'clonic' type of innervation of cerebral origin, which was responsible for voluntary movement, while there was also a 'tonic' type, involving a different group of muscles and probably regulated from the cerebellum. He believed that 'the cerebellum is the centre for continuous movements and the cerebrum for changing movements. Thus in walking the cerebellum tends to stiffen all the muscles; the changing movements of walking are the result of cerebral discharges overcoming in a particular and orderly way the otherwise continuous cerebellar influence.'

In his studies of muscular movements Charles Beevor drew attention to the importance of synergic fixation and analysed the manner in which it was produced; while, from the point of view of experimental physiology, Sherrington has given us a minute analysis of the factors concerned in the co-ordination of muscular movement. To the English reader familiar with this large and fundamentally important body of work, it must come as a great surprise that none of it appears as yet to have influenced German neurology. Indeed, Strümpell complains that physiologists have not paid any attention to the static aspects of motor innervation, which have been left to the modern neuropathologist to discover and analyse.

He proceeds to give a clinical application of his view. He regards paralysis agitans and the other rarer forms of 'extrapyramidal motor disease' as examples of disorder of myostatic innervation, or as forms of an 'amyostatic symptom complex'. When myostatic innervation is continuously hyperactive (how or why we are not told) we get the rigidity of paralysis agitans. When it is only rhythmically increased, the tremor of this disease results, while, when the hyperactivity is irregular in both force and frequency, we see athetosis. The various sources of fallacy to be detected in these applications of his views were discussed in the review referred to above.

F. M. R. W.

Moore, Lillian M. Experimental studies on the regulation of the body temperature. III. The effect of increased intracranial pressure on body temperature. *Am. J. Physiol.*, 1919, **50**, 102.

In heat puncture experiments on rabbits it was found that there was no correlation between the location of the lesion and the occurrence of hyperthermia. The experimental evidence of the existence of special centres in the brain for the heat regulation of the body is therefore not confirmed.

By increasing the intracranial pressure, hyperthermia is produced. In the so-called 'heat puncture' experiments, the hyperthermia is probably due to haemorrhages from the cranial vessels. The increased pressure produces bulbar stimulation and thus excitation of the vasomotor centre. The resulting vaso-constriction leads to a diminution of the heat loss.

W. C.

May, E. S. and **Lassen, J. A. Posture sense conduction-paths in the spinal cord.** *Am. J. Physiol.*, 1919, **50**, 204.

Dogs were trained to take food only when the right hind leg was held in a certain position—that of rigid extension backwards. When training was complete hemi-section of the cord was performed at different levels, as follows:

Dog. 1.	Right	hemi-section,	level of	first thoracic.
Dog. 2.	Right	,,	,,	last thoracic.
	Right	,,	,,	first lumbar.
Dog. 3.	Right	,,	,,	first thoracic.
	Left	,,	,,	first lumbar.

In every case response to posture tests remained prompt and decided after the operation. It is concluded that part of the fibres conveying posture sense impulses decussate within the cord. Some of the impulses probably travel back and forth across the cord at different levels by short association fibres.

W. C.

PATHOLOGY AND BACTERIOLOGY

Twort, F. W. An investigation on the nature of ultra-microscopic viruses. *Lancet*, 1915, ii, 1241.

d'Herelle, F. (1). Sur un microbe invisible antagoniste des bacilles dysentériques. [**An invisible microbe antagonistic to dysentery bacilli.**] *Compt. rend. Acad. d. sc.*, 1917, **165**, 373.

d'Herelle, F. (2). Technique de la recherche du microbe filtrant bactériophage (*Bacteriophagum intestinale*). [**The method for demonstrating the filterable microbe *Bacteriophagum*.**] *Compt. rend. Soc. de biol.*, 1918, **81**, 1160.

d'Herelle, F. (3). Sur le microbe bactériophage. [**The 'bacteriophage' organism.**] *Compt. rend. Soc. de biol.*, 1919, **82**, 1237.

d'Herelle, F. (4). Sur la culture du microbe bactériophage. [**The cultivation of the 'bacteriophage' organism.**] *Compt. rend. Soc. de biol.*, 1920, **83**, 52.

d'Herelle, F. (5). Sur la résistance des bactéries à l'action du microbe bactériophage. [**The resistance of bacteria to 'bacteriophages'.**] *Compt. rend. Soc. de biol.*, 1920, **83**, 97.

Kabéshima, T. Sur un ferment d'immunité bactériolysant, du mécanisme d'immunité infectieuse intestinale, de la nature du dit 'microbe filtrant bactériophage' de d'Herelle. [**A bacteriolytic ferment in immunity, the mechanism of immunity against intestinal disease, the nature of d'Herelle's 'bacteriophage'.**] *Compt. rend. Soc. de biol.*, 1920, **83**, 219.

During the course of investigations into filterable viruses, Twort, in 1915, made cultures on agar of glycerinated calf lymph, and after incubation observed the development of 'watery-looking areas'. If cocci grew in such tubes, they were often found to be dead on subculture and, if kept, the colonies became transparent and glassy. A healthy colony touched with some of the glassy material soon began to become glassy. This action is more active upon young vigorous cultures and is entirely absent from dead cultures.

Some of the glassy material, diluted 1 in one million and filtered, was still able to prevent growth of the cocci on agar or to dissolve it if grown. This 'condition or disease of the micrococcus' may be carried from culture to culture for an indefinite number of generations, but the glassy material itself does not grow on any medium, although if inoculated into a tube it will retain its activity for over 6 months.

It is clear that the glassy material contains an enzyme, which is destroyed at 60° C. This enzyme increases in quantity when placed in an agar tube containing micrococci and so can be carried on indefinitely. The author discusses whether the glassy material is a stage in the life cycle of a micrococcus or whether it is an enzyme secreted by the micrococci which leads to their own destruction. He favours the latter view. Since the effect can be propagated through generations of healthy cocci, 'it might almost be considered as an acute infectious disease of micrococci'.

A large number of other experiments were made, and similar enzymes were found in distemper and infantile diarrhoea.

This dissolving enzyme may account for some of the difficulties in isolating certain bacteria.

d'Herelle, 2 years after Twort, discovered in the faeces and urine of cases of dysentery an invisible microbe which had a marked antagonistic action upon Shiga's dysentery bacillus. The faeces were inoculated into broth, incubated for 18 hours, and then filtered through a Chamberland candle. A small quantity of the filtrate added to cultures or suspensions of Shiga's bacillus dissolved and killed them in a few hours. A trace of this killed culture had the same effect upon a fresh suspension or culture, and the first strain had been carried in this way through 50 generations. At first the invisible virus only acted upon Shiga's bacillus, but later it developed the same action upon Flexner or Y bacilli, losing thereby its effect upon Shiga. It had no effect upon other bacteria. The virus was nonpathogenic to animals. A similar invisible organism was isolated from 2 cases of typhoid and showed a lytic action upon *B. paratyphosus A.*

This is a new genus of microbe and is termed *Bacteriophagum,* the antidysentery variety being named *Bacteriophagum intestinale.* By means of collodion filters its size is estimated to be no larger than a protein molecule. It is living, having now been propagated for 935 passages.

In addition to the antidysentery and antityphoid-group bacteriophages, the author isolated varieties antagonistic to a number of other intestinal bacteria, namely *B. coli,* hog cholera, &c.

The author again returns to the question of whether the lytic action is due to a lysin produced by his bacteriophage or whether the lysin is not produced by the lysed bacterium itself under the influence of an unspecific cause x. He favours the original view as the result of various considerations of an indirect nature.

The author has isolated a large number of strains of his bacteriophage, but has never found two to be identically the same; he appears to lean to the idea that there is really only one strain which is capable of adapting its lytic action to the flora it happens to meet with in the intestine.

The bacteriophage withstands a temperature of 65° C. and can only exert its action upon living bacilli.

The later notes contain mostly theoretical considerations relating to the virulence of the bacteriophages and the mechanism of infection and resistance or struggle between bacteriophage and bacillus.

Kabéshima disputes the contention of d'Herelle that his 'bacteriophage' is a living virus, because it will withstand heating to 70° C. Further, the fact that a very minute quantity of filtrate will dissolve a large number of bacteria in a few hours and the fact that it can be kept at room temperature for 4 years without undergoing deterioration are more suggestive of a ferment.

He succeeded in precipitating the ferment from the filtrate of faeces with acetone as a white powder. It could not therefore be a living organism. He looks upon the substance as a catalyst which causes micro-organisms to produce autolytic ferments; these ferments act as catalysts to other bacteria, and so the lytic action can be carried from generation to generation. The catalyst is produced by the dysenteric or typhoid patient as a protective measure against infection.

It is clear that both Twort and d'Herelle are describing exactly the same phenomenon, viz., a character which may be obtained from calf lymph or faeces, which has a lytic and destructive effect upon bacteria. This effect can be propagated indefinitely through pure cultures of the *living* bacteria, but will not grow on any medium. Although Twort refers to the lysis as 'an infective disease of the cocci', he is of opinion that it is due to an autolytic enzyme produced by the bacteria themselves. In the absence of any knowledge as to the nature of filter-passing organisms, he does not exclude the possibility that his enzyme is a filterable virus, 'an enzyme with power of growth'.

d'Herelle, on the other hand, frankly accepts the idea of a living filterable virus, but it would appear from the work of Kabéshima that this view is hardly tenable, unless of course we have to do with some borderland variety of life with which we are not at present familiar. P. F.

Noguchi, H. (1). **Etiology of yellow fever. IV. Acquired immunity of guinea-pigs against *Leptospira icteroides* after the inoculation of blood of yellow fever patients.** *J. Exper. M.*, 1919, **30**, 1.

Noguchi, H. (2). **V. Properties of blood serum of yellow fever patients in relation to *Leptospira icteroides*.** *J. Exper. M.*, 1919, **30**, 9.

Noguchi, H. (3). **VI. Cultivation, morphology, virulence, and biological properties of *Leptospira icteroides*.** *J. Exper. M.*, 1919, **30**, 13.

Noguchi, H. (4). **VII. Demonstration of *Leptospira icteroides* in the blood, tissues, and urine of yellow fever patients and of animals experimentally infected with the organism.** *J. Exper. M.*, 1919, **30**, 87.

Noguchi, H. (5). **VIII. Presence of a Leptospira in wild animals in Guayaquil and its relation to *Leptospira ictero-haemorrhagica* and *Leptospira icteroides*.** *J. Exper. M.*, 1919, **30**, 95.

Noguchi, H. (6). **IX. Mosquitoes in relation to yellow fever.** *J. Exper. M.*, 1919, **30**, 401.

Noguchi, H. (7). **X. Comparative immunological studies on *Leptospira icteroides* and *Leptospira ictero-haemorrhagica*.** *J. Exper. M.*, 1920, **31**, 135.

Noguchi, H. (8). **XI. Serum treatment of animals infected with *Leptospira icteroides*.** *J. Exper. M.*, 1920, **31**, 159.

The first three papers of this series have been reviewed already (vide this Journal, 1919, **1**, 114).

The blood of yellow fever patients has very little pathogenicity for guinea-pigs. Signs of disease were only noticed in 8 out of 74 animals; however, all upon subsequent inoculation with thick suspensions of *Leptospira icteroides* were found to be immune against infection, although animals treated with malarial or normal blood were not immune.

Pfeiffer's reaction, using the serum of patients convalescent from yellow fever and cultures or suspensions of *L. icteroides*, was found to be positive in 83 per cent. The serum of such patients had also a protective action for guinea-pigs against inoculation with *L. icteroides*. These observations suggest strongly that *L. icteroides* is aetiologically related to yellow fever.

L. icteroides was cultivated 3 times out of 11 directly from cases of yellow fever by means of Inada and Ido's technique for *L. ictero-haemorrhagica*. These cultures transmitted a characteristic disease to guinea-pigs and was recovered from the blood of these animals. The Leptospira passes the pores of a Berkefeld filter.

L. icteroides can be found in the blood of yellow fever patients with the dark-ground illuminator (3 times in 37).

67 per cent. of mice and wild rats in Guayaquil were found to be infected with *L. ictero-haemorrhagica.* Immune sera were prepared in rabbits with these strains and were found to confer only slight protection against infection with *L. icteroides.* It is therefore concluded that *L. icteroides* differs from *L. ictero-haemorrhagica.*

Stegomyias engorged with blood of yellow fever patients or of guinea-pigs infected with *L. icteroides* produce in guinea-pigs a disease resembling yellow fever. This result is, however, very infrequent. The incubation is much longer with Stegomyias fed on man than upon animals. Further experiments are described to determine whether *L. icteroides* is the same as *L. ictero-haemorrhagica.* Monovalent agglutinating sera for *L. icteroides* have a slight or no action on *L. ictero-haemorrhagica.* Similarly, there is a slight cross-agglutination of *L. icteroides* strains. Further, Pfeiffer's reaction and protection was exhibited against both organisms by one serum, although more intensely against the homologous strain.

A polyvalent immune serum was of definite advantage in the treatment of animals infected with *L. icteroides.*

The crux of this series of papers, in which a new organism (*Leptospira icteroides*) is advanced as the cause of yellow fever, is whether this new organism differs from *S. ictero-haemorrhagica,* the cause of Weil's disease. It would appear that the demonstrable differences are no greater than may be found between two strains of meningococci, and thus the two spirochaetes must be of the same genus ; in which case doubt must exist as to whether the 'disease known as yellow fever in Guayaquil' was true yellow fever at all. If it was, yellow fever must have a very close aetiological relationship with Weil's disease. P. F.

Pease, M. C. The bacteriology of infectious gaseous gangrene. *Proc. Soc. Exp. Biol. and Med., N.Y.*, 1919, **17**, 30.

This is a short statement concerning the bacteria which cause or are associated with gas gangrene. The author divides the microbes which have been found into three main categories. (1) Essential causal agents which are divisible into a saccharolytic group including *Vibrion septique, B. oedematiens,* and *B. welchii,* and a proteolytic group, the only representative in which is *B. histolyticus.* (2) Accessory agents of gaseous gangrene. Here also there are two main divisions, viz., anaerobes and aerobes. The anaerobes are proteolytic (*B. sporogenes* and *B. aerofoetidus*), or saccharolytic (*B. fallax*). The aerobes include *B. coli* and *B. proteus,* although the author considers it doubtful whether these can be regarded as true causal agents. The third main group are never essential causal agents, though they may be capable of causing complications and many have an importance in symbiosis with other agents. Among these are anaerobes and aerobes. The former includes *B. putrificus, B. bifermentans, B. tetani,* and *B. tertius,* while the aerobes include cocci (Streptococci, staphylococci, and diplococci), bacteria (*B. proteus, B. coli, B. pyocyaneus*), and bacilli (*B. anthracoides, B. subtilis, B. mesentericus,* and *B. mycoides*).

The author comments on the great variations of virulence, and remarks that under exceptional circumstances *B. sporogenes, B. fallax,* and *B. aerofoetidus* may produce a lesion by themselves, although they are commonly associated with others of greater pathogenicity. He refers to an analysis of 308 cases of gas gangrene, of which 91 were derived from Weinberg's series and 217 from wounded American soldiers. The percentage incidence of the various anaerobes was:

B. welchii .	85	per cent.
B. sporogenes .	35·4	,, ,,
B. oedematiens	12·6	,, ,,
Vibrion septique	17·2	,, ,,
B. fallax . .	6·4	,, ,,

In this series only 79 cases were due to one single pathogenic microbe, the remaining 229 having from two to six anaerobes in the local lesion. The author also considers that on account of the difficulties of isolation the above percentages do not represent the real incidence of the different types.

W. B.

Schranz, F. Ein Fall von tödlich verlaufener Gasphlegmone nach Coffeininjection. [**A fatal case of gas phlegmon following injection of caffein.**] *Med. Klin.*, 1920, **16**, 182.

Attention has already been directed (*Medical Science*, 1920, **1**, 442) to thirteen cases of fatal gas phlegmon following the subcutaneous injection of caffein. The present author reports still another, viz., a strong girl aged 21 who received an injection of caffein in the thigh. She was suffering from influenza and pneumonia. Immediately after the injection she complained of local pain, and an area of redness made its appearance, and in about seven hours the whole thigh swelled and was crepitant. Discoloration of the skin set in, not only on the thigh but also on the breast, cheeks, and forehead, and she died early the following morning of *foudroyant* gas phlegmon. A partial autopsy revealed lesions from which *B. welchii* was recovered. The caffein solution, which was obtained from the hospital dispensary, was not examined.

W. B.

Schürer, J. Ueber die Pathogenese der Dauerausscheider und Bazillenträger. [**On the pathogenesis of the permanent bacillary carrier.**] *Berl. klin. Wchnschr.*, 1920, **57**, 106.

The author considers that infective diseases may be subdivided into two groups. In the one the infective process, in the event of recovery, comes to an end after a relatively short space of time—measured by weeks. Cholera, plague, relapsing fever, measles, German measles, typhus fever, chicken-pox, and variola belong to this group and do not give rise to a chronic carrier state. The second group comprises particularly diphtheria, typhoid fever, dysentery, and probably scarlet fever. After the acute general symptoms have subsided, chronic local inflammatory processes may persist for long periods discharging the specific virus outwards to promote new infections. Epidemiologically, new outbreaks of the diseases in the first group occur from patients or recent convalescents, whereas the diseases of the second group may and do frequently occur from persons apparently perfectly healthy. This process may go on for years till the disease becomes endemic.

W. B.

Lewis, P. A. and **Dodge, F. W.** **The sterilization of lipovaccines.** *J. Exper. M.*, 1920, **31**, 169.

The authors point out that the method of preparation of lipovaccines does not assure the sterility of the finished product. Further, the presence of the oil interferes with the action of antiseptics so that these cannot be depended on for final sterilization. They have used heat applied to the finished vaccine as a means of sterilization and have tested the antigenic properties of the resultant vaccine.

Working with a pneumococcus lipovaccine they find that a temperature of 130° C. for 3 hours or 120° C. for 12 hours does not destroy the antigenic properties. In these experiments mice were protected against 10 fatal doses when the lipovaccine had been given 38 days previously. When, however, the interval was 21, 56, or 110 days, there was no evidence of protection. The immunity conferred by these vaccines therefore appears to be singularly transient.

Typhoid lipovaccine was tested in the same way, but its antigenic properties were found to be destroyed by the heating. G. T. W.

Conn, H. J., Harding, H. A., and **Kligler, I. J.** [et al.] **Methods of pure culture study. Progressive report for 1918 of the committee on the descriptive chart of the Society of American Bacteriologists.** *J. Bact.*, 1919, **4**, 107.

This Committee report is divided into four parts:

1. The descriptive chart and its purpose. A historical account of the origin of this chart and its chief objects are given, followed by a criticism of its value.

2. The Gram stain. The technique of two different methods is given, the criticism of the Society upon them being invited, with the idea of obtaining a standard technique.

3. The production of acid. The followings points are considered:
   - (*a*) Sources of error in determining acid production.
   - (*b*) Media recommended.
   - (*c*) Methods of detecting acid production.
   - (*d*) H-ion concentration—its relation to acidity, the meaning and measurement of P_H.
   - (*e*) Why the titration method is illogical.

4. The reduction of nitrates. The Committee is unable at present to propose a standard method for its determination, but a provisional procedure is recommended. W. A. M. S.

Buchanan, R. E. Agglutination. *J. Bact.*, 1919, **4**, 73.

This is the presidential address delivered before the Society of American Bacteriologists and is particularly directed to certain physico-chemical conceptions and their bearing on a theory of agglutination. There is first a historical survey of the work done by different investigators in the phenomenon of bacterial agglutination. Then follows a discussion as to why bacteria agglutinate, and the questions of cataphoresis and sensitization. With regard to denaturation or sensitization, the following factors influencing it are considered in detail with special reference to experimental work:

1. Nature and composition of antigen.
2. Adsorption of other colloids, and of non-electrolytes.
3. Adsorption of electrolytes—hydrogen-ions, cations (univalent, di-, tri-, and polyvalent).
4. Relation of valency to power of agglutination.
5. Denaturation by non-colloids.
6. Graphic representation of action of mixtures.

It is concluded that bacterial agglutination is a colloidal phenomenon, best studied in the light of modern work on colloidal and physical chemistry. The need for a more intensive study of the question is emphasized and the putting of the diagnostic use of agglutination on a more scientific basis.

W. A. M. S.

Clark, P. F. and **Ruehl, W. H.** **Morphological changes during the growth of bacteria.** *J. Bact.*, 1919, **4**, 615.

The authors seek to obtain additional information in regard to possible cyclical changes in the growth of bacteria by making repeated microscopic examinations of organisms at intervals of one to three hours for 24 hours after transplanting, and at longer intervals for a week or more. Great attention was paid to the purity of the original cultures, and to uniformity of technique in dealing with them. In all, 70 strains were used, comprising 37 species. They were selected from most of the recognized groups of pathogenic bacteria.

In all cases (except among members of the diphtheria group and possibly *B. mallei*) the young organisms found in cultures from 4–9 hours old were much larger than those from 20 to 24 hours old. In some cases the difference is great enough to render the organisms unrecognizable when viewed by the ordinary standard of the 24-hour culture. The period of largest organism formation closely corresponded to the period of rapid cell division.

In the diphtheria group the young organisms in cultures of 4–9 hours old were definitely smaller and showed more 'solid staining' than the older forms; the average size in cultures of this age being less than in old cultures showing involution forms. In the other groups the senile forms were always the smallest.

Graphs are shown representing growth curves—length of bacteria in microns being plotted against time in hours. A series of photo-micrographs shows the differences in the morphology of different organisms from cultures of various ages.

W. A. M. S.

McIntosh, J. and **Smart, W. A. M.** **The determination of the reaction of bacteriological culture media.** *Brit. J. Exp. Path.*, 1920, **1**, 9.

This paper is divided into the following parts:—

1. An explanation of the more important features of the ionic theory, in order to understand the symbols and nomenclature now used in reference to the reaction of culture media.

2. Methods of measurement of hydrogen-ion concentration—by the hydrogen electrode and by the use of indicators.

3. An investigation of the sources of error in estimating the P_H values of media, under the following heads:—

(*a*) Alteration of the reaction due to heating by steaming and by autoclaving.

(*b*) Difficulty of judging the 'end-point' of the indicator selected.

(*c*) Titration at boiling-point and at room temperature.

4. The establishment of a relationship between the Eyre notation and the hydrogen-ion concentration. Phenolphthalein and thymolphthalein

are used as indicators, and the above relationship is shown by a set of graphs suitable for laboratory use.

5. Procedure suggested for the preparation and standardization of ordinary broth.

6. Recommendations. For routine purposes the authors recommend the estimation of the reaction of the bacteriological media by titration of a small volume and calculation from the result, of the amount of alkali required to be added to the remainder. The final reaction is adjusted by addition of N/1 HCl. They find that the most suitable indicator is thymolphthalein, for it changes at a point on the alkaline side of neutrality sufficient to ensure the precipitation of phosphates. The 'end point' chosen is the first perceptible darkening on the addition of alkali, the titration being performed in the cold.

As a final control they suggest the use of two indicators—cresol red and phenolphthalein. W. A. M. S.

MacLean, H. and **de Wesselow, O. L. V. On the testing of renal efficiency with observations on the 'urea coefficient'.** *Brit. J. Exper. Path.*, 1920, **1**, 53.

This paper begins with a criticism of the methods of determining the condition of the kidneys in patients suffering from renal disease. The urine of 10,000 newly joined recruits was examined, also that of 50,000 apparently fit soldiers who had just completed their training. The amount of albumin, its association with casts, the amount of blood urea, and the use of dyes are all considered. The authors found that when a large dose of urea was given to a patient with defective kidneys, the patient was unable to excrete urine with a high urea concentration. Also the degree of this concentration appears to be directly related to the kidney involvement. They maintain there is but little trouble in the use of the test, no special apparatus or facilities are required, the urea produces no untoward symptoms, and can easily be carried out in general practice or in hospital wards. The Ministry of Pensions is using their method—a complete scheme of their routine examination of the renal condition being given. MacLean's modification of Ambard's formula is used, viz. $Ur / \sqrt{D\sqrt{c}/W}$, where Ur is the weight (in grams) of urea per litre of blood, D the weight of urea excreted per 24 hours, C the weight of urea per litre of urine, and W the weight of the patient in kilograms. The various factors here involved are examined in detail, and a criticism of the value of Ambard's 'coefficient of urea excretion' is offered. In the opinion of the authors their new test of renal efficiency (inability of the diseased kidney to excrete urea at a high concentration) is of more value in indicating deficiency of the kidney function than others now in use. W. A. M. S.

Meyerhof, K. Meningitis typhosa oder Meningotyphus? [**Typhoid meningitis or meningotyphoid?**] *Berl. klin. Wchnschr.*, 1920, **57**, 132.

Typhoid meningitis may occur as a metastatic complication of a general typhoid sepsis or the condition may be a primary one—meningotyphoid—the blood and intestinal tracts being free of typhoid bacilli. The author describes two rare cases which almost certainly belong to the latter class.

In one, the patient was admitted with bronchitis, but on manifesting symptoms referable to the nervous system a lumbar puncture was made and in bile, cultures revealed typhoid bacilli, although the blood cultures made a few days previously were negative. The patient who recovered had been inoculated against typhoid, and the author suggests as an explanation of the typhoid bacilli in the cerebrospinal fluid that the bacilli may have been killed by the antibacterial substances in the blood, which substances were however absent in the C. S. F.

The second case was an extremely severe one and ended fatally with leptomeningitis, hydrocephalus, hyperaemia and oedema of the brain. During life blood cultures were negative, whereas typhoid bacilli were found in the C. S. F. The author emphasizes the necessity of incubating cultures in bile for several days before reporting that they are sterile, and he also points out the advantage of diluting the blood in bile more than is usually considered necessary. W. B.

Bennett, C. B. and **Schmidt, L. A.** **On red cell globulin.** *J. Immunol.*, 1919, **4**, 29.

The nature of the actual antigenic substance in the red cells which causes a production of haemolysins when injected into animals has long been a subject for discussion. It has been attributed to the haemoglobin, the insoluble stroma or the lipoids.

The present authors tested the CO_2 precipitable globulins to see whether these had antigenic value and also to compare them with the similar globulin in the serum of the same species.

Oxalated ox blood was centrifuged and the corpuscles washed with saline. The deposited corpuscles were then laked with two volumes of water and centrifuged to remove stroma. The fluid was then diluted 10 times with water and saturated with CO_2 until the globulin separated in large flakes. The globulin was washed and dissolved in saline. A similar globulin was also prepared from ox serum.

Rabbits were then immunized with the red cell globulin and fixation experiments were carried out, using the red cell globulin and the serum globulin as antigens. Positive fixations were obtained with red cell globulin but not with the serum globulin, showing a specific antibody production by the red cells. It was next demonstrated that the rabbit serum was haemolytic to ox cells to a high titre in the presence of complement and agglutinating without complement. The antigenic fraction of red cells is, therefore, either the globulin of the red cells or some other body intimately associated with it. P. F.

Bayliss, W. M. **Is haemolysed blood toxic?** *Brit. J. Exper. Path.*, 1920, **1**, 1.

Statements which have been made that haemolysed blood is toxic when injected into an animal are rendered doubtful by the fact that most of the experiments have been performed on rabbits which are specially susceptible to intravascular clotting.

One-third of the volume of a cat's blood was withdrawn and the blood-pressure maintained by an injection of gum saline. The blood was defibrinated, laked by freezing and thawing and reinjected. The urine was deeply stained with haemoglobin, but no toxic signs appeared.

Haemolysis *in vivo* was brought about by injecting a quantity of warm tap water equal to the calculated quantity of blood. The fluid rapidly left the circulation, and although there was no fall in blood-pressure the quantity of urine excreted was much diminished. This was counteracted by the injection of sodium chloride to make the plasma isotonic, the salt concentration being diminished by dilution with the tap water.

It was found that haemoglobin in the circulation was capable of carrying oxygen. Dale and Richards showed that histamin produced a dilatation of the capillaries if blood corpuscles were present, and the author found this to be true, using haemoglobin instead of blood.

When toxic results follow the injection of haemolysed blood, these are to be ascribed to the effect of foreign protein. P. F.

Sachs, H. Zur Frage der Brauchbarkeit cholesterinierter Organextracte für die Serodiagnostik der Syphilis. **The value of cholesterin in the antigen in the serum-diagnosis of syphilis.** *Deutsche med. Wchnschr.*, 1920, **46**, 60.

It appears that Hatziwassiliu has stated that the addition of cholesterin to an antigen for use in the Wassermann reaction 'greatly increases the non-specific inhibitory power, so that undoubtedly negative sera with cholesterin give positive Wassermann reactions'.

Without bringing forward any new grounds in support of cholesterin, the author states that this criticism is without foundation.

Although in Germany the technique of the Wassermann reaction seems to be still in a state of flux, the author has, perhaps without knowing it, the support of the great majority of workers in Great Britain and America.
P. F.

Fildes, P. The serological classification of meningococci. *Brit. J. Exper. Path.*, 1920, **1**, 44.

This paper is a further study of the value or correctness of the classification of meningococci by serological methods. The author concludes that while two main serological types exist, which do not depend upon an arbitrary selection of standard strains, there are insufficient grounds for describing four types. The two extra types described by Gordon are not distinctly separable from the two main types and can only be separated by an arbitrary selection of standard cultures. P. F.

Brownlee, J. An investigation into the epidemiology of phthisis in Great Britain and Ireland. Part III. *Medical Research Committee, Special Report Series*, 1920, **46**.

This publication contains the completion of Dr. Brownlee's investigation into the epidemiology of phthisis in Great Britain. It begins with some mathematical sections necessary for the argument, but from the ninth section onwards the discussion does not involve any knowledge of mathematics. It is found, as shown in Part I, that the influence of hygiene as measured by the standard death-rate is in very close relationship with the amount of phthisis at 'middle age'. Among males in London especially, the correspondence is absolute. Whether the figures for the whole of London for the six decades for which statistics are available, or whether the figures for the individual boroughs of London for the years 1911–1914 (the only years for which the deaths are accurately given for the respective boroughs) are taken, the same relationship is found. Thus the fall in the amount of phthisis in London from 1850 to the present day is measured exactly by the fall in the death-rate. The same relationship is shown to hold for Glasgow. When, however, the districts in which phthisis in youth and phthisis in old age, typified by Wales and Cornwall respectively, are examined it is found that the fall in the amount of phthisis is quite independent of the death-rate from all other causes, this death-rate remaining practically constant in these districts during the period at issue. Further, when analysis of the relative amounts of 'young adult', 'middle age' and 'old age' phthisis in England is made, it is found (1) that 'young adult' phthisis in both sexes has very greatly declined: (2) that 'middle age' phthisis in males is about the same at present as it was in 1850, having risen to a maximum about 1875 and then declined, the process following the course of the death-rate from all other causes between the ages of 35 and 55: that 'middle age' phthisis in females declined, slowly at first and then more rapidly, following again the course of the death-rate from all causes among females between 35 and 55 years (thus the course has been different in the two sexes, but both agree with the course of general mortality in the respective sexes): (3) that the amount of phthisis at old age is about half what it was in 1850, but this fall shows no association with the death-rate at high ages.

Dr. Gordon's figures regarding the relationship of phthisis to exposure to wind are then discussed and his results subjected to some statistical analysis. Some addition to his facts has been made by taking out the number of deaths from phthisis in the office of the Registrar-General for periods for which Dr. Gordon gives no statistics. The results show that essentially the same phenomena existed in the earlier epochs as at the present. It is found that in these districts which Dr. Gordon examined much the largest amount of phthisis is in the young adult.

Proceeding from wind to sub-soil an examination of the facts in Norfolk, Suffolk, and Essex is given, which shows that there is a certain amount of correlation between the amount of boulder clay present in a district and the amount of 'young adult' phthisis, but that there is no relation between the sub-soil and the amount of 'middle age' phthisis. It is to be noted that the same difference is found in Essex which lies on two clays—the boulder and the London clay. The phenomena is not due therefore to clay soil, but is associated with a specific kind of clay. Dr. Buchanan had already shown that on the London clay there was a tendency to have less phthisis than on other sub-soil. Further investigation of this subject in the northern counties of England is promised.

Migration is then considered, and it is shown to be probable that migrants from country to town suffer less from phthisis than those born in the town. The data are not very satisfactory. In the case of Glasgow, in which the birthplaces of more than 2,000 cases of phthisis are recorded, the rate of notification per 1,000 persons born outside the city is 3·5 as against 7·0 among those born in the city.

A note on tuberculosis at early ages follows in which it is shown that the greater the amount of tuberculosis at ages under 5 years, the less the amount of phthisis at the 'young adult' ages, and the greater the amount at 'middle' ages. There is no relationship to the amount of 'old age' phthisis. It is also found from the data given by the Medical Officer of Health for London with regard to the sources of the tubercular milk sent to the city, that in those counties from which the milk comes there is a very high correlation between the deaths from infantile tubercle and the proportion of the tubercular milk dispatched. On the other hand there is a very high negative relationship between the quality of tubercular milk and the amount of 'young adult' phthisis. 'Middle age' phthisis again is associated with tubercular milk.

A discussion of phthisis in Wales of some length is then given. It is shown that in Wales the amount of 'young adult' phthisis is much greater upon the Ordovician strata, but this is not necessarily directly associated with the geological formation as the social conditions differ very markedly.

It thus seems that the influences which favour 'young adult' phthisis are opposite to those which favour 'middle age' phthisis. Two explanations of these facts seem possible. The first is that there are at least two distinct strains of the bacillus of tubercle, each of which has special ages of selection. One attacks in early adult life and old age, the other in childhood and middle age. The one is associated with the country and the other with the town. The second explanation is that the response of the human organism to the bacillus may be physiologically different according to the environment. On this hypothesis prevalence of tuberculosis in childhood establishes immunity in young adult life in those who survive. Further, when the strain of life in towns begins to tell, persons at those ages at which the strain is most felt, namely those between 40 and 50 years, tend to succumb. In the country the health of persons at these ages is good and consequently death from phthisis is rare. Wind, wet, bad feeding probably tend to make the youth adult specially susceptible to phthisis. The author prefers the first theory that phthisis is not one disease but a mixture of several diseases.

J. B.

Cesaris-Demel, A. Les plaquettes. Recherches sur leur origine, etc. [**The blood-platelets, their penetration into the vessels, and the variations in shape which they show.**] *Arch. ital. de biol.*, 1919, **69**, 223.

After paying a tribute to the work of Wright and his theory of the origin of the blood-platelets, the author gives his own conclusions.

(1) The blood-platelets, though independent elements, cannot be considered as cells since they lack a nucleus.

(2) They originate mainly from the azurophilic protoplasm of the megacaryocytes, in part also from other elements of the spleen representing earlier stages of the megacaryocyte.

(3) They originate from the megacaryocytes by a differentiation and detachment of small masses of protoplasm, either from the periphery of these cells or from the extremity of a pseudopod. These pseudopodia either penetrate directly into the capillaries and then give off platelets, or the megacaryocyte remains extra-vascular, or again the whole cell may pass into the vessel as a leucocyte in diapedesis and there breaks up into platelets, the nucleus being carried on as an embolus to the pulmonary capillaries.

(4) Normally the platelets are almost identical in shape and size, but if the process of differentiation is accelerated by toxins of chemical or bacterial origin irregularities in the size and form of the platelets occur. Such anomalies are especially seen in myeloid leukaemia. H. M.

McConnell, G. The delayed negative Wassermann reaction. *J. Lab. and Clin. M.*, 1919, **5**, 41.

The delayed reaction occurs when haemolysis occurs only after half an hour after adding the haemolytic system.

Of 18 such cases, in the frankly syphilitic cases it was found that of 8, 7 had had antisyphilitic treatment previously. In 6 questionable cases all denied syphilis, but each had a gonorrhoeal history. In the other 4 cases no history of lues was obtainable. C. G. L. W.

Benjamin, J. E. and **Havre, S. J. Further observations on the relation of aortic insufficiency to the Wassermann test.** *J. Lab. and Clin. M.*, 1919, **5**, 47.

Wassermann reaction examined in 33 cases of aortic insufficiency, only 11 per cent. gave a positive W. R. Undisputed histories of rheumatism were obtained in 57 per cent. of the cases. C. G. L. W.

Blatz, W. E. A review of recent literature bearing on the function of the thymus gland. *J. Lab. and Clin. M.*, 1919, **5**, 50.

A review with references to recent papers. C. G. L. W.

Macklin, C. C. Development and function of macrophages in bone wounds in rats vitally stained with trypan blue. *Carnegie Lab. of Embryol., Johns Hopkins Hosp. Contribution to Embryol.*, 1919, **27**, 46. (*Physiol. Abstracts*, 1920, **4**, 478.)

In the healing of bone wounds macrophages which stain with trypan blue congregate, grow and exercise phagocytic power. They develop from lymphocyte-like cells from the blood-stream and also from mononuclear cells with phagocytic potentialities. Their special use is the removal of waste products, including bone, cartilage, if present, and the result of breakdown of other tissues as the result of injury. C. G. L. W.

BIOCHEMISTRY

Luckiesch, M. Infra-red radiant energy and the eye. *Am. J. Physiol.*, 1919, **50**, 383.

The author deals with the problem whether the absorption of the infra-red radiant energy by the eye media is responsible for eye fatigue and for glass-workers' cataract. He does not declare either for or against this view, but points out that at present infra-red radiation stands convicted, not upon experimental evidence, but only upon circumstantial evidence which is, moreover, not convincing. The object of this paper is to show in what relative quantities the energy is absorbed in the various parts of the eye, and thus to furnish data for the further consideration of the problem. The author's computations are based on the experimental observations of Aschkinass, who found that the various eye media transmitted the visible and infra-red rays in the same manner as like thicknesses of water. The author finds that when viewing luminous objects of small area (subtending a small solid angle) there is no serious concentration of energy in the eye media until the retina is approached. When viewing extended objects (large solid angle) there is a relatively much greater energy density in the lens and anterior parts of the eye than in the posterior portions. This indicates that large sources of radiation of a relatively low visual brightness might be effective in forming cataract or causing eye fatigue, if the 'absorption of energy' theory is correct. It is pointed out, that if the deterioration of the lens is due to ultra-violet rays, the latter might be present in such small amounts as to appear harmless, but when it is recalled that the energy density is very high when viewing extended objects, such as the sky, pavements, surfaces of molten glass, metal, &c., it appears to be possible that the ultra-violet rays still might be present in sufficient amount to do damage. From this standpoint sunlight, owing to the greater intensities encountered, appears to be probably as effective in producing cataract and eye fatigue as ordinary artificial illuminants and some industrial processes. W. C.

Krabbe, K. H. Early synostosis of the epiphyses with dwarfism in pubertas praecox. *Endocrinology*, 1919, **3**, 459.

The case is one of a girl 13½ years old, who first menstruated when she was a few months old, and has menstruated regularly every four weeks ever since. She has had several haemoptyses which, in the absence of a demonstrable lung disease, may perhaps be looked upon as a vicarious menstruation. The axillary and pubic hair is well developed and her breasts have always been abnormally large. She grew rapidly up to the age of 7 years and was then strikingly tall. Since then growth has wholly stopped, and her limbs are now abnormally short in relation to the trunk. Her mentality corresponds to her age, which distinguishes this case from many other cases of pubertas praecox. X-ray examination showed that in the upper and lower limbs the epiphyses had grown together. This synostosis took place probably at the age of 7–8 years, when growth stopped. A comparison is drawn with the few other cases of pubertas praecox where an X-ray examination was made.

The case is of interest as exhibiting both dwarfism and sexual precosity. As a case of dwarfism it differs from that associated with thyroid and pituitary diseases where the epiphyseal fissures remain open for an abnormally long time but where there is a diminished proliferation at the epiphyseal lines. The early synostosis in this case suggests a hyperactivity of the ovarian internal secretion. The sexual precosity might be due to a tumour either of the pineal gland, the ovary, or of the adrenal cortex. A tumour of the pineal gland can be definitely excluded in this case. Large tumours of the adrenal or ovary can also be excluded. And although small benign tumours of these glands might be the cause, the author is inclined to attribute the condition to an abnormally early function of the internal secretion of the ovary, similar to the hypersecretion of the thyroid in Graves's disease. W. C.

Gordon, M. B. The rôle of the pineal in pediatrics. *Endocrinology*, 1919, **3**, 437.

The paper gives a critical account of the present state of our knowledge—or rather ignorance—of the function of the pineal gland, together with references to the literature, most of which has been published during the last two or three years. Among many contradictory observations a few facts stand out as fairly well established. The gland undergoes retrograde changes early in life, the age at which these changes begin in man being fixed by some at 7 years, by others at puberty. It is not essential to life, for it can be removed without affecting the well-being of the animals. The operation is technically difficult, and observation in which severe symptoms followed the removal of the gland are probably vitiated by the occurrence of injuries incident to the operation, especially haemorrhage from the veins and sinuses around it. Some observers have found that removal of the gland in young animals was followed by an accelerated sexual development in the males, but not in the females. Dandy, working with puppies, failed to find any difference between operated animals and the controls, and doubts whether the gland has any endocrine function of importance. The administration to young animals of pineal extracts from young bullocks, either by the mouth or by injection, has in the hands of some observers been without effect, while by others it has been found to produce a more rapid increase in weight and to hasten sexual maturity, especially in the males. This latter fact is obviously difficult to reconcile with the observations referred to above, in which a similar effect was produced by removal of the gland. It is further stated that in puppies there was a perceptible difference in the intelligence as the result of pineal feeding, the pineal fed puppies being one month ahead of the controls in their habits. Observations have been made on the effect of pineal feeding in mentally deficient children, and it has been claimed that in cases of simple retardation without organic changes an improvement was detected.

Perhaps the most suggestive evidence that the pineal gland has an endocrine function is furnished by the symptoms associated with pineal neoplasms. Apart from neurological symptoms, which are not specific and are those usually found as a result of intracranial pressure from any tumour of the midbrain, there are characteristic metabolic symptoms, when the disease affects the gland before puberty, as it frequently does (17 cases out of a total of 60 cases were in children under the age of 14). The metabolic symptoms are: (1) adiposity ; (2) sexual changes, namely, an early sexual and mental development and a general body overgrowth, so that a child of 5 or 6 may have the appearance of one of 11 or 12 ; (3) cachexia. The cachexia is perhaps a secondary effect of the hydrocephalus or the tumour, and may have no relation to the pineal. Even the adiposity and the sexual changes may not be produced directly by changes in the function of the gland, but may be referred to interference with the pituitary gland as the result of pressure.

As the result of a large number of autopsies on cases of mental disorders, histological changes in the pineal gland have been described in certain types of insanities (dementia praecox, primary and secondary amentias). An attempt has been made to establish a relation between the pathology of progressive muscular dystrophy and changes in the pineal gland as seen by X-ray examination of the skull.

In concluding his interesting paper with a consideration of the function of the pineal body, the author states that our knowledge of its function is 'more problematic than accurate'. W. C.

Meulengracht, E. Den kliniske Betydning af Undersögelsen for Galdefarvestof i serum. [**The clinical significance of examinations of the serum for bile pigment.**] *Ugesk. f. Læger*, 1919, **81**, 1785–99.

Meulengracht finds that tests for bilirubin in the blood dependent on extraction are too complicated for the clinician, and may even be less accurate than simpler methods. The procedure he has elaborated is in principle the same as that devised by Hoover and Blankenhorn, and more recently by Nyström. The colour of the bilirubin itself, not that of a new chemical union with bilirubin as a component, is estimated colorimetrically by a simple process of dilution. The reliability of this test depends on the absence from the serum of other substances than bilirubin with a yellow colour. For practical purposes this postulate is fulfilled in man, although in certain animals the serum contains other substances with the same colour as bilirubin.

Technique. Three c.cm. of blood, taken from a vein in the arm, are introduced into a small Wassermann tube containing a few drops of a 20 per cent. solution of sodium citrate. Sedimentation of the blood cells is effected by standing for some hours or by centrifugalization. One c.cm. of the supernatant serum is then drawn off (with a pipette fitted with a long tube so that the exact position of the point of the pipette can easily be seen) and introduced into a test-tube in which it is diluted with a 0·9 per cent. solution of sodium chloride until its colour coincides with that of the standard colour solution contained in a test-tube of the same size. The comparison is best made against a white background. The diluting fluid required to bring the colour of the serum to standard is now measured in c.cm. The standard solution is one of potassium bichromate ($\frac{1}{10000}$) or of chloride of iron ($\frac{1}{300}$). This standard solution is called 1, and its colour is the pale yellow of normal serum. The number of c.cm. of the diluting fluid required to bring the serum to standard colour is the dilution or bilirubin number. This is between 10 and 20 in persons with merely a suspicion of jaundice of the skin, and it may be between 200 and 300 when jaundice is intense. The standard solution of chloride of iron is apt to darken on standing, whereas the colour of the potassium bichromate keeps well.

Meulengracht's clinical material begins with a group of 40 healthy persons, most of whose sera were under 1. In some cases the colour of the serum was deeper than standard, being 3 to 4. At this figure Gmelin's serum reaction begins to be positive. Up to the figure 4, bilirubinaemia may be physiological. Bilirubinaemia was uniformly present in cases of croupous pneumonia, but never in rheumatic fever even when the temperature was high. This suggests that the nature of the infecting organism, rather than the height of the fever, determines the development of bilirubinaemia, which is analogous in many respects to the albuminuria of febrile diseases. Bilirubinaemia may be classified according as it is (1) febrile or toxic, (2) due to stasis, as in heart disease with cardiac failure, (3) due to haemolysis, as in chronic, hereditary haemolytic jaundice (among the 40 cases of this disease the dilutions varied between 3 and 41, being usually between 10 and 20), or (4) due to obstruction, as in disease of the liver and bile-ducts. The highest figure reached was 250, in a case of pancreatitis.

In a comparison of the three conditions bilirubinaemia, jaundice, and bilirubinuria, it is pointed out that the first is by far the earliest manifestation of an excess of bilirubin in the body. Indeed, the concentration of bile pigment in the serum must reach a considerable degree before jaundice is visible, and a still higher concentration before bilirubinuria is demonstrable. Thus the serum dilution in several cases was as high as 10 without any sign of jaundice, and bilirubinuria was never demonstrable before the serum dilution had reached about 50. Sometimes it was even as high as 130, and the lowest figure associated with bilirubinuria was 48. It is a work of supererogation to examine for bilirubinuria, because jaundice of the skin is provoked by a much smaller concentration of bilirubin.

Bilirubinaemia having been shown to be the earliest and most easily measured of the three manifestations of excess of bilirubin, it is of great diagnostic value when jaundice is very slight and its presence is in doubt. The pigmentation may seem equally deep in two cases of jaundice, but the bilirubinaemia figure may be 100 in one case, 200 in the other. The bilirubinaemia figure also shows whether the condition is increasing or decreasing, whereas changes in the degree of jaundice are notoriously difficult to detect. In the differential diagnosis of cancer of the pancreas and gall-stones, Meulengracht has noticed that in the former the increase of bilirubin is more uniform than in the latter. His method is also useful in the differential diagnosis between haemolytic and other forms of anaemia. The former is associated with bilirubinaemia, which is absent if the anaemia is due to reduced production of red cells. Thus there is more or less bilirubinaemia in the pernicious anaemias, none in the chloroses or anaemias of haemorrhage. In certain cases of cardiac insufficiency with oedema, albuminuria, &c., bilirubinaemia may show that the symptoms are due to stasis in the hepatic system, whereas if it is absent these symptoms should rather be traced to renal disease. Again, the demonstration of bilirubinaemia is of great diagnostic value when the obstruction caused by the passage of gall-stones is too brief to provoke jaundice or bilirubinuria, giving rise only to bilirubinaemia. In another class of case, the patient may give a history of brief and recent jaundice. This may have vanished, but the correctness of the patient's statements can be checked by testing for bilirubinaemia. This is also instructive in the case of young adults who for years are subject to transitory bouts of slight jaundice of obscure origin. In half a score of these cases, the bilirubinaemia figures ranged from 5 to 10.

C. L.

Osborne, T. B. and **Mendel, L. B. Do fruits contain water-soluble vitamine?** *Proc. Soc. Exper. Biol. and Med.*, 1919, **17**, 46.

Fresh apples and pears prevent loss of weight when vitamine-free diets devoid of water-soluble vitamine are used. The inner peel of the orange contains these substances. The proportion is not large.

C. G. L. W.

Halsey, R. H. Profound effects of digitalis on the vagus, producing severe detrimental subjective symptoms as shown by simultaneous electrocardiograms and pneumograms. *Proc. Soc. Exper. Biol. and Med.*, 1919, **17**, 36.

In a case of syphilis, chronic interstitial nephritis, dilatation and hypertrophy of the heart, auricular fibrillation, arteriosclerosis, periodic breathing of the Cheyne-Stokes type in which, because the auricle was fibrillating, digitalis was given in order to slow the ventricle. The ventricle was contracting 100 times per minute during apnoea, and slowed to half that rate as soon as hyperpnoea began. As digitalis was continued, distress was caused which was most severe during hyperpnoea. The ventricle rate did not become slower. By releasing the heart from vagus control by giving gr. $\frac{1}{30}$ of atropin, the patient became more comfortable. It is concluded that digitalis did not improve the circulation because of its effect on the vagus, interfering with the CO_2 and O_2 exchange between the blood and the alveolar air. C. G. L. W.

Field, C. W. Blood-sugar curves with glucose, lactose, maltose, mannite, and cane sugar. *Proc. Soc. Exper. Biol. and Med.*, 1919, **17**, 29.

One hundred grams of the pure sugar in a large glass of water were given and the sugar content of the blood tested, one, two, and three hours after ingestion.

The glucose curve had its apex in the first hour, maltose gives the same curve as glucose. Mannite gives a similar curve, but the apex is not so pronounced. Cane sugar has its apex in the second hour. Lactose only shows a slight rise at the end of the second hour. C. G. L. W.

RADIOLOGY

Radio-diagnosis

Fournier. Un cas d'achondroplasie : antécédents familiaux d'hypothyroïdisme. [**A case of achondroplasia with known antecedents of hyperthyroidism.**] *Anales de la Facultad de Medicina*, 1918, Jan. and Feb., 892. (*J. de radiol. et d'électrol.*, 1918, **3**, 138.)

The patient was a youth of 15, suffering from achondroplasia, whose two uncles and an aunt had shown more or less grave symptoms of hypotrophy. The radiograph reveals the following anomalies: the lower extremity of the radius is increased in size, the junction of the diaphysis and the epiphysis is more perfect than is usual in a normal person at that age. The lower extremity of the radius is equally augmented in size, as well as the styloid process.

The union between epiphysis and diaphysis is complete. The carpal and metacarpal bones and the phalanges are enlarged and shortened. The fourth metacarpus is a little shorter than the others (Levi's sign). In the lower limbs the extremities of the bones are enlarged, the condyles of the femur being large, irregular, the protuberances prominent with persistence of the cartilage. The tibia is incurved, the union of epiphyses and diaphyses are complete. The head of the fibula reaches to the level of the articular space. At the hip, the upper edge of the great trochanter is at the same level as the head of the femur which is oval and enlarged. The cotyloid cavity has little depth, the ilium is thickened and squat. Amongst the many theories advocated to explain these lesions F. gives his opinion in favour of internal hypersecretion of the genital gland in a person in a state of congenital hypotrophy. As a matter of fact, the generative precocity of the patient, his great development of hair and muscle, and the general appearance of masculinity seem to support the view. W. S. L.-B.

Keppler and **Erkes.** Zur Röntgendiagnostik beim Divertikel der Speiseröhre. [**Radio-diagnosis of diverticula of the oesophagus.**] *Med. Klin.*, 1919, **15**, 480. (*Zentralbl. f. Chir.*, 1919, **46**, 777.)

The authors, after observing two cases in which carcinoma was found after the diagnosis had been given as oesophageal diverticulum from the X-ray plate, looked through the X-ray literature from the point of view of mistakes and found that among the 250 hitherto published cases of oesophageal diverticulum the X-ray plate had proved misleading in seven. The cases are shortly described and discussed. Even after close examination it appears that in the given cases, errors in the diagnosis could hardly have been avoided, yet knowledge of the fact is of importance.

S. U. L.-B.

Déjerine, Mme et **Ceillier, M. A.** Para-arthropathies du genou chez les paraplégiques. [**Conditions surrounding the knee-joint in paraplegia.**] *Rev. Neurol.*, 1918, Nos. 11–12, 348. (*J. de radiol. et d'électrol.*, 1919, **3**, 374.)

This paper deals with the juxta-articular osteophytes of the knee in paraplegia after traumatic lesion of the spinal cord. Radiography is the essential element of the diagnosis. It enables one to see that the osteophytes are exclusively extra-articular and appear to begin at the level of the internal condyle. The osteophytes, in number from 3 to 6 and of the shape of an egg or a button, surround the condyle without fusing with it; they are often bilateral. By radiological examination it is seen that the morphologic integrity of the femur is complete, the new bony formations have no relations to the skeleton except that of position : this enables one to diagnose the condition from rheumatoid arthritis in which, according to Barjou, there are skeletal lesions and disappearance of the interarticular spaces. On the other hand, there is a close analogy between para-arthropathies in paraplegia and the true arthropathies of tabes and syringomyelia. 'By means of early radiographs one could distinguish the pre-arthritic stage of tabes.' At this stage, in many cases, the lesions will, no doubt, be mainly articular.

S. U. L.-B.

Dandy, W. E. Röntgenography of the brain after the injection of air into the spinal canal. *Ann. Surg.*, 1919, **70**, 397.

Dandy's X-rays of the air-filled lateral ventricles often showed a network of light lines over the hemispheres. These were first interpreted as the grooves in the bone made by the cranial vessels. Later, it was recognized that they were produced by air which had escaped from the fourth ventricle and was now lying in the subarachnoid channels over the sulci. Dandy has attempted deliberately to bring about such a distribution of injected air with a view to establishing the permeability or otherwise of the subarachnoid spaces in suspected cases of hydrocephalus. In this he has met with a certain measure of success, although some of the radiograms reproduced are so heavily retouched as to make them valueless to those who might wish to form an unbiased opinion. However, the technique of the method is simple, and all may form their own conclusions from actual experiment. Lumbar puncture is performed in the usual manner with the patient sitting, and air, equal in volume to the fluid withdrawn, carefully injected. The air is neither filtered nor sterilized. In 8 cases so treated by Dandy there were no ill effects whatever in 6, 1 had a headache which lasted 3 hours, and 1 vomited. The sulci appear as a network of fine lines over the hemispheres; in 24 hours all signs of the air have gone, whither, it is not known. The value of the method is in the localization of obstructions in the cerebrospinal river bed. In 3 out of the 8 cases the site of the obstruction was accurately determined: (1) an obstruction due to adhesions in the cisterna pontis, causing hydrocephalus, (2) blocking of the hemispheral furrows by adhesions in a patient recovered from cerebrospinal meningitis and now hydrocephalic, (3) tumour of the mid-brain, air-block at anterior end of cisterna pontis.

Dandy suggests that the method may also be of value in the localization of spinal tumours. It might be dangerous in cerebral neoplasms.

G. J.

Gaillado et **Cornil.** Variations de l'ombre cardiaque à la radioscopie durant la compression oculaire. [**Variations of the cardiac shadow in radiography during ocular compression.**] (1) *Compt. rend. Soc. de biol.*, 1918, March. (2) *Presse méd.*, 1918, March. (*J. de radiol. et d'électrol.*, 1918, **3**, 140.)

The authors have made the following observations:

(1) Between the 10th and the 20th second of compression the edge of the left ventricular shadow is displaced progressively outwards, its maximum of dilatation being attained from the 30th to the 45th second. On cessation of the compression the left shadow returns little by little to its original limit in a period varying from 30 to 50 seconds.

(2) The modification concerns the entire ventricular border in 71·5 per cent. of cases, the lower three-quarters in 11·5 per cent., its lower half in 17 per cent. The displacement varies also in respect of its situation: maximum in the middle part of the left ventricular border (54·8 per cent.); minimum in the region of the apex (29·1 per cent.); the dilatation of the middle part equal to that of the apex (16·1 per cent.).

Finally, its intensity varies between 2 and 13 mm. The verification of this left ventricular dilatation could perhaps be otherwise made by measuring the volumetric ventricular angle before and during the compression.

W. S. L.-B.

Tribout, F. Examen radiologique des biloculations de l'estomac et des résultats opératoires. [**X-ray examination of hour-glass stomach and the operation results.**] *Thèse pour le doctorat*, 1919, Paris. (*J. de radiol. et d'électrol.*, 1919, **3**, 375.)

The radiological examination of hour-glass stomach ought to be carried out from two distinct points of view, (1) morphologically, by the immediate examination in the upright and horizontal position, (2) physiologically, by the emptying time.

The differentiation between true and false hour-glass stomach is relatively easy. One must exclude the biloculation due to an atonic stomach the subject of ptosis, and also biloculation from extrinsic causes such as compression by liver, spleen, glandular enlargements, mesenteric tumours, distension of the large intestine, or from the presence of perigastric adhesions.

The spasmodic forms are less easily diagnosed. In these cases, the spasm accompanies a pyloric or parapyloric lesion, or a lesion of the cardia. In certain cases, one may try to allay this spasm by the subcutaneous

injection of atropin sulphate for 24 hours and examining within 3 hours after the last injection. Sometimes this routine will cause the spasm to disappear.
R. W. A. S.

Duval, P. A propos des aspects biloculaires de l'estomac à l'examen radiologique. [**X-ray examination of hour-glass conditions of the stomach.**] *Arch. des mal. de l'appar. dig. et de la nutrit.*, **3**, 163. (*J. de radiol. et d'électrol.*, 1919, **3**, 374.)

Bilocular conditions of the stomach are due either to anatomical causes or to transient alterations in outline.

There are two main classes.

1. The group without actual stenosis which is transient in character. It includes:

(*a*) atonic biloculation;
(*b*) biloculation from compression;
(*c*) „ „ spasm.

2. Biloculation from definite stenosis of the body of stomach which is recognized by the following characteristics:

Persistence of the condition in all positions, under manual palpation or with insufflation of the stomach.

The appearance, at the moment of taking the opaque meal, of a single pouch, then after some time a streak of bismuth which goes on to fill a lower pouch.

Several examinations may be necessary before a diagnosis is arrived at. The author thinks it essential for the surgeon to be present at the examination before deciding upon operative interference.

R. W. A. S.

Radio-therapy

Nordentoft, S. Om Behandlingen af Mb. Basedowii. [**X-ray treatment of Graves's disease.**] *Ugesk. f. Læger*, 1919, **81**, 1169–75.

In 1918 Nordentoft published 50 cases of Graves's disease treated with X-rays in the period July 1915–December 1917. His present paper deals with a new series of 50 cases, only three of which were males. At the Aalborg Kommune Hospital the practice has been adopted of exposing only the region of the thymus to the X-rays. He gives a few illustrative cases, but does not attempt to tabulate or classify his results, confining his estimate to general terms. He is greatly impressed by the efficacy of this treatment, with which better results can be achieved than with any other. He urges its adoption at an early stage before the disease has got well established, and he advocates large and few doses in preference to small and frequent doses. With the adoption of this principle, and the inclusion of the thymus in the area exposed, he anticipates that severe and fatal cases of Graves's disease will become so rare that many medical men will never see them. Discussing X-ray fatalities in connexion with Graves's disease, he suggests that timid dosage may partly be responsible, and he quotes Forsell in support of his hypothesis that the small dose merely stimulates, whereas the large dose inhibits the activities of the thyroid. He also notes that in certain fatal cases of Graves's disease death probably occurred in spite of, not because of, the X-ray treatment.
C. L.

Mühlmann, E. Zur Röntgenbehandlung der Lymphdrüsentuberkulose. [**X-ray treatment of tuberculosis of the lymphatic glands.**] *Deutsche med. Wchnschr.*, 1918, **44**, 994. (*Zentralbl. f. Chir.*, 1919, **46**, 340.)

Among the civil population lymphatic gland tuberculosis usually arises from a general tubercular tendency; among soldiers, on the other hand, one sees the worst masses of glands, almost without exception, in strong healthy men whose general health is always good. Frequently the condition is combined with other tubercular affections, e.g. lung, larynx, lupus, &c. The author observes that otherwise entirely healthy, strong men bearing enlarged glands are exactly those who are unusually resistant to the rays. The highly-filtered rays of modern deep therapy are too intensive and penetrating for the smaller and medium-sized tumours. Smaller quantities and weaker filtering should be sufficient from a purely physical point of view. One cannot hope for 100 per cent. of cures from X-ray treatment. Still, the number of the author's cases which had to be operated upon is small and decreasing. Prophylactic irradiations increase the formation of fibrous tissue in the covering of the gland and check recurrence, and a similar result can also be favoured by post-irradiation. If the gland masses after five or six irradiations within a period of 15–18 weeks have not receded sufficiently, the remainder of the glands must be removed by operation. If the skin be to some degree capable of resistance the author advises the method advocated by Seeman, viz. sterile puncture of the gland abscesses followed by the injection of a 10 per cent. iodoform-glycerine solution. Tuberculosis of the lymphatic glands is not merely a local, but is a general disease. So that the whole range of tuberculosis therapy must be brought into the treatment of these patients.

S. U. L.-B.

Radium Therapy

Heyman, J. Om radiumhemmets resultat med behandling av livmoderkräfta under 1914 och 1915 bedömt efter 5 års observationstid. [**Radium in cancer of the uterus. Results 5 years later.**] *Svenska Läk. Sällsk. Förhandl.*, 1919, **12**, 394–7.

Heyman's 'autoreferat' of a paper read at a meeting of the Svenska Läkaresällskapet shows that 26 cases of cancer of the cervix were treated at 'Radiumhemmet' in 1914, and 40 in 1915. Of the 1914 cases, 7 were alive on November 1, 1919, and of these again, 5 were inoperable, 1 was operable, and 1 was a borderland case in 1914. Of the 1915 cases, 11 were cured. The percentages of cures, as judged by survival for 5 years after treatment, were thus 26·9 and 27·5 for the 2 years. The uniformity of these results in the two years diminishes the chances of their being more or less fortuitous. In 94 per cent. of the cases the disease was inoperable, and if the results achieved in the 3 'clinically' operable, the 1 'technically' operable, and the 5 borderland cases be judged by themselves, the proportion of cures becomes 44·4 per cent. Heyman observes that operative treatment seldom effects more than 20 per cent. of cures, and that with radium treatment the high operation mortality of surgical treatment is avoided. He gives no technical details, merely referring to Forsell's methods, which, he says, if adopted put the treatment of cancer by radium at least on a level with that of operative treatment. At the discussion which followed it was pointed out that Heyman had understated his case for radium, as his figures referred mainly to inoperable cases, whereas the successes achieved by surgery concerned early operable cases. C. L.

Bertolotti, M. Radiumterapia nei tumori ipofisari a sindrome acromegalica. [**Radium therapy of tumours of the hypophysis, with syndrome of acromegaly.**] *Radiol. med.*, 1919, **6**, 315.

A number of cases have now been treated by radiation with some favourable results, and a notable improvement in several. As there is great variation in the symptoms according to the position of the tumour this may account for variation in the results of treatment, and the negative results of X-ray therapy in some cases. In distrophy from tumour of the hypophysis the author's own results have been unfavourable; similarly the clinical results of all tumours are varied, and the course of the disease may be from 2 to 59 years. In benign cases X-rays are advisable and useful. The detractors of X-rays assert that the improvement is a natural retrogression, but this is always of short duration, whereas the improvement after X-rays lasts much longer. The best results are obtained in early cases, and, as cystic degeneration follows in acromegaly, X-rays should be applied before this sets in. The author gives the history of a case treated by the gamma-rays of radium from the early days.

The first symptoms were seen in May 1917, and by December the condition was already far advanced — vision nearly gone, impotency, asthenia, &c.—so that an adenoma or adeno-carcinoma of the pituitary was suspected, most probably of the anterior lobe and of rapid and malignant development. A course of intensive radium treatment was begun, but by March, after two treatments, the patient was worse instead of better and the condition seemed desperate. Not till July was there a slight improvement, when the vision of the left eye began to increase. Continuous though slow progress was made, and in September the radiograph showed surprising improvement in the profile of the sella turcica.

By December 1918 the vision had so far recovered that the patient was able to resume his work as a designer, and all the symptoms had disappeared. This result was obtained solely by massive doses of radium applied bi-temporally, and neither the intrabuccal nor the intranasal method was employed. It follows that the rays are efficient at a distance of more than 10 cm. through tissues, and have probably an elective action on certain neoplastic cellular elements. N. H. M. B.

MEDICAL SCIENCE

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REVIEWS

CARDIO-VASCULAR DISEASES

In his thesis on **dextrocardia** Duval states that up to 1909 210 cases had been published. Culcer-Petresco in a Paris thesis in 1913 collected 58 cases recorded between 1896 and 1912, in 20 of which the dextrocardia was an isolated phenomenon and in the rest associated with total inversion of the viscera. Duval has collected 71 cases of dextrocardia with total inversion of the viscera and 6 of pure dextrocardia from the literature published between 1912 and 1919. He notes that some writers have actually denied the existence of congenital dextrocardia apart from complete inversion of the viscera, but he brings forward the following arguments in favour of an isolated congenital dextrocardia: (1) The presence of dextrocardia in a perfectly healthy individual without any previous history of pleuro-pulmonary disease indicates a congenital malformation, whereas an individual whose present condition may be satisfactory, but who has a previous history of respiratory disease, is probably the subject of acquired dextrocardia. (2) In acquired dextrocardia it is the rule for the axis of the heart to retain its normal orientation, the organ being displaced as a whole, the base being most to the right, the apex below and to the left, and the long axis of the heart being directed from above downwards and from right to left. On the other hand, in pure congenital dextrocardia the long axis is directed from left to right, from above downwards, and from within outwards as in complete inversion of the viscera. (3) In the electrocardiogram of congenital dextrocardia, as shown by Nicolai in 1911 and Neuhof in 1913, the peaks of the three waves are inverted.

Parsons-Smith records four cases of dextrocardia in soldiers aged from 19 to 31, in two of whom the transposition affected not only the heart but the liver and stomach as well, and in the others, was associated with a normal situation of these organs. He regards dextrocardia without transposition of viscera as of serious moment, as symptoms of incompetence, such as dyspnoea, palpitation, insomnia, faintness, and pain are bound to occur sooner or later as the result of a general visceral overcrowding, the liver impeding the movements of the heart and the upper lobes of the right lung. The pains of which the patients complain are both local and referred, local when they denote pressure upon the intercostal nerves or brachial plexus, referred when the vagus or its intracardiac endings suffer inordinate stimulation. Dextrocardia without transposition of the viscera is usually complicated by actual malformation of the heart and great vessels, such as pulmonary stenosis or atresia, transposition of the great vessels, incomplete septa or patent ductus arteriosus. In one of the writer's cases it was considered that the ventricular septum was perforate. On the other hand, when it is associated with complete transposition of viscera dextrocardia does not incapacitate and is usually only discovered by accident.

According to an editorial annotation in the *Lancet* of December 13 there was no note of the occurrence of dextrocardia among the quarter of a million men placed in Grade IV nor among the 16,000 men in each of the three higher grades. On the other hand, three cases were observed during the examination of 20,000 men at Liverpool.

Braun reports a fatal case of **gonococcal endocarditis** in a man aged 54 which developed during treatment for a recently acquired gonorrhoea. At the autopsy ulcerative endocarditis of the aortic valves was found, a pure culture of gonococci being obtained from the valvular lesions.

According to Nobécourt, who records a case of chronic **tuberculous endocarditis** in a boy aged 13, tuberculous lesions of the endocardium may assume various forms. Anatomically specific lesions such as isolated or miliary tubercles are exceptional, whereas lesions apparently identical with those of ordinary endocarditis, single or ulcerative, are more common. Ulcerative endocarditis is found fairly frequently in autopsies on phthisical subjects. In a certain number of cases they are due to secondary infection, but occasionally tubercle bacilli may be found on microscopical examination on inoculation of the guinea-pig. Simple tuberculous endocarditis is not uncommon, the naked eye and microscopical lesions resembling those of rheumatic endocarditis. They are usually situated on the mitral valve and often on the tricuspid and aortic valves as well. According to Braillon simple tuberculous endocarditis is more localized than rheumatic endocarditis and does not present the oedema and interstitial infiltration found in the latter. Tuberculous endocarditis may occur in patients who have other tuberculous lesions, like Nobécourt's case in which spina ventosa. Pott's disease and signs of tracheo-bronchial adenopathy and mediastinitis were present. Sometimes, however, the endocarditis is primary, and occurs in patients who have no clinical signs of tuberculosis. In such cases the endocarditis shows an attenuated character like other forms of local tuberculosis, especially sero-fibrinous pleurisy. It is liable, however, to end in chronic endocarditis, giving rise to mitral incompetence or less frequently aortic insufficiency. The gravity of tuberculous endocarditis is the tendency, especially in children, for it to be associated with tuberculous lesions of the mediastinum and pericardium and for early and progressive loss of compensation to result.

Pardee made a study of cases of valvular disease at the Military Heart Hospital, Colchester, 19 of whom had aortic regurgitation and two of them aortic stenosis also, while 22 were considered to have mitral stenosis. He found that the best conditions for hearing the murmur of mitral stenosis were present after exercise, and especially when lying on the left side after exercise. Without exercise the left lateral and the bent forward positions were by far the most favourable. The dorsal position was better than the erect in about 45 per cent., though in 36 per cent. it was less favourable. The best conditions for hearing the murmur of aortic regurgitation were the erect bent forward position, the erect position in forced expiration and the erect position after exercise. The murmur was found to vary only in intensity and not in quality. At times it was not heard with the ordinary stethoscope, but could be heard with the ear directly against the chest wall. Very faint murmurs due to aortic regurgitation were heard near the sternum in the fourth left interspace, the third left interspace or the second right interspace.

In patients with aortic disease Zak describes an area of flushing, shaped like a half moon with the corners about the middle of the clavicles and the convexity falling over the sternum. In some cases it is an erythema, in others it resembles a slight sunburn but limited to the characteristic area. Occasionally it has a butterfly distribution. There is no parallel between its intensity and the severity of the aortic disease. By comparison with healthy men the capillaries in this area are found more sensitive to mechanical stimuli so that the half-moon flush over the upper part of the sternum may even be induced by brushing the arm. The sign depends upon a spinal reflex comparable with that underlying a hyperalgesic area; it is an objective Head's zone.

Weiser describes a new sign of tricuspid insufficiency, which he had observed in two cases, viz., pulsation of the eyeballs. It developed during failure of compensation and disappeared as the heart's action became stronger. The following explanation of the phenomenon is given. In tricuspid insufficiency a portion of the contents of the right ventricle is driven with each systole through the auricle into the jugular vein and thence into the cavernous sinus and orbital veins. As the heart becomes stronger the valve closes better, less blood enters the venous system, and the pulsation of the eyeballs ceases.

The recent paper by Zondek, on the heart in **coal-gas poisoning** (vide *Medical Science*, 1920, **1**, 475) induced Liebmann of the Zurich University Medical Clinique to record a fatal case in a woman, aged 38, the autopsy on whom showed the presence of severe interstitial and parenchymatous myocarditis. He attributes the clinical symptoms, viz., fall of blood-pressure, arrhythmia, and cardiac dilatation, to the presence of these lesions.

Alexander records a case of **pericardial effusion** due to the presence of cholesterin in a man aged 32 who showed signs of hypothyroidism. Over three pints of a dark brown fluid of scintillating gold paint appearance were withdrawn. The cardiac condition rapidly improved and recovery took place.

Disordered action of the heart. Wearn and Sturgis studied the reaction to the intramuscular injection of a small dose (0·5 c.c. of a 1 : 1000 solution) of epinephrin in normal soldiers and in a group of soldiers with symptoms of 'irritable heart'. Of 26 normal soldiers who had gone through a very severe army training for 14 months not one gave a positive reaction as judged by observation of the pulse-rate, blood-pressure, objective signs or symptoms. Of 73 patients with symptoms of 'irritable heart' about 60 per cent. gave a reaction which definitely indicated a hypersensitiveness to epinephrin, viz., rise of blood-pressure, increased pulse-rate, restlessness, nervousness, praecordial pain, palpitation and tremor. Although it might be supposed that the symptoms and signs in the positive cases were the result of a hypersensitive sympathetic autonomous nervous system, examination showed that there were no essential clinical differences between the two groups.

In a subsequent paper Tompkins, Sturgis, and Wearn record the effects of intramuscular injection of epinephrin on the basal metabolism in soldiers with 'irritable heart', in hyperthyroidism and in normal men. In all three groups epinephrin caused an increase in total gaseous metabolism, but the increase in metabolism was greater in cases showing a positive reaction to epinephrin. There was an increase in the minute volume of air breathed under the effects of epinephrin, and of either respiratory rate or depth, or both. After intramuscular injection of epinephrin there was very frequently an elevation of respiratory quotient, the maximum of elevation usually preceding that of the metabolic increase.

Clough studied the effect of epinephrin on the electrocardiogram of patients with 'irritable heart', and in some cases observed gross abnormalities of the electrocardiographic record. Changes in conduction (delayed conduction, partial heart-block) and the production of ventricular extra systoles were the most important deviations from the normal. No changes were found in the conduction time or the length of systole in epinephrin hypersensitive patients or in normal men. In both at the height of the reaction there was a decrease in the height of the T wave. An attempt was made to correlate the symptoms complained of by patients with 'irritable heart' at the height of the reaction with abnormalities of the electrocardiogram, but no definite association could be found.

Bridgman, while on duty at a convalescent camp in France, analyzed 5,000 case histories of patients presenting the effort syndrome. 91 per cent. of these were sent back to full duty and 3 per cent. were returned to base hospitals for operation or treatment which would probably later allow their discharge to Class A. Every patient was studied for symptoms of hyperthyroidism. Only three cases of exophthalmic goitre were found among the 5,000, and besides these only an occasional soldier showed struma, adenoma, diarrhoea or any eye signs beyond a slight von Graefe.

Sturgis, Wearn, and Tompkins of the cardio-vascular division of the Medical Service, U. S. Army General Hospital No. 9, Lakewood, New Jersey, gave subcutaneous injections of atropin sulphate 1·2 mg. to 10 normal men and 21 soldiers with irritable heart with the following results. In both groups there was generally a preliminary drop followed by an increase in pulse-rate. This increase was greater on the average in the 'irritable heart' cases than in the normal controls. There was also a drop in pulse-pressure dependent upon a rise in diastolic blood-pressure in the majority of cases and upon an additional drop of systolic blood-pressure in some of the cases. There was no increase in basal metabolism, but in three of the six cases studied there was a slight fall. There was always a slight drop in the respiratory quotient.

Exact observations upon the **circulation during fainting** have seldom been recorded. Common difficulties are its unexpectedness and the absence of apparatus. Cotton and Lewis availed themselves of the special opportunities in a military hospital for heart cases. The premonitory symptoms, such as dizziness and disturbed vision, are attributable to the same cause as the subsequent loss of consciousness, namely, deficient blood-supply to the cerebrum. There is a form of transient dizziness, not of the same nature as that premonitory of syncope, where change of posture is the chief exciting cause and the pulse-rate may be increased or unchanged. But in the cases of actual syncope reduction of rate occurred almost invariably; it fell either from a previous relatively high rate to the normal or from normal levels to 50, 40, or even 30, a minute. The gradual fall of rate conditions the premonitory symptoms, and then the unconsciousness. The force of the heart-beat is also reduced, for the sum is an actual fall of systolic blood-pressure during the bradycardia. Readings of 60–70 mm. Hg were obtained and below this the pulse was very small or imperceptible. This contrasts with the maintained pulse level seen in tracings of syncope due to auriculo-ventricular block, which was absent in the cases here described. The association of reduced rate and lowered force of the heart-beat, and the subjoined gastric symptoms, show that ordinary fainting attacks are of vagal origin, and atropin effects prompt recovery.

Cardiac tumours. According to Norton, who reports a case of myxoma of the heart simulating broncho-pneumonia in a man aged 29, myxomata form about 30 per cent. of all primary tumours of the heart. The symptoms of cardiac tumours as described by him are dyspnoea, general weakness, anaemia, depressed mental condition, palpitation of the heart, a low-tension pulse, and variability of all signs and symptoms. Norton agrees with Victor Petit in emphasizing the intermittent character of the symptoms of cardiac tumours. Organic heart lesions like stenosis or insufficiency do not produce symptoms one day only to disappear on the next. The variability of the symptoms must depend to some degree upon the position of the tumour with reference to the blood-flow, and if the pedicle is long, the variability depends upon a torsion of the pedicle. The tumour in Norton's case filled the left auricle and presented polypoid growths, one of which bulged the fossa ovalis into the right pulmonary vein and another protruded into the mitral orifice.

According to Göttel of the Pathological Institute of Greifswald University there are no symptoms peculiar to cardiac tumours. Either they remain latent owing to their small size and position and are discovered merely by chance, or they grow against the valves and simulate a valvular lesion, or else they cause symptoms suggestive of mediastinal tumour or an aneurysm. Of the few specimens of cardiac tumours which have been collected in the Greifswald Pathological Institute within the last 50 years only three gave rise to clinical symptoms. The first case, which occurred in a girl aged 12, was a lymphosarcoma of the thymus which invaded the cardiac wall and compressed the superior vena cava, giving rise to oedema of the face and distension of the veins of the upper part of the body. The second case, which occurred in a woman aged 39, who had been delivered three months previously, was a syncytioma of the left ventricle with embolism of the left Sylvian artery giving rise to hemiplegia. Both these cases were examples of secondary heart tumours. The third case, which was a primary tumour of the heart, was a round-celled sarcoma of the septum of the right auricle in a woman aged 62, in whom the diagnosis during life was thrombosis of the superior vena cava.

Pommay-Michaux and Boué report a case of spindle-celled sarcoma of the heart secondary to sarcoma of the pleura in a man aged 58, the myocardium being to a great extent destroyed by the growth.

At a meeting of the Medico-Chirurgical Society of Pavia on August 8, Arrigo reported a case of **hypertrophic lymphangioma** of the aorta in a girl aged 14 who had died of naso-pharyngeal and laryngo-tracheal lupus. The anterior surface of the aorta within the pericardium showed two small tumours the size of a lentil which on histological examination were found to consist of newly-formed lymphatic capillaries which had developed mainly round the vasa vasorum in the adventitia of the aorta. They were lined with cubical or cylindrical endothelial cells and contained lymphocytes or a granular substance. Arrigo regarded these small growths as hypertrophic lymphangiomas closely allied to lymphangio-endotheliomas, and especially to their perivascular form.

West records a case of **stenosis of the aorta** of Bonnet's adult type in a labourer aged 50 who died suddenly while suffering from empyema. He had had no previous illnesses. The cardio-vascular signs were a systolic murmur at the base and dilated varicose vessels pulsating beneath the skin in the region of the vertebral border of the scapula. At the necropsy the constriction which was at the site of attachment of the ligamentum arteriosum was found to be abrupt and of an hour-glass type. The constricted portion was from one to two millimetres in diameter. The aorta was of about normal size from its origin to the origin of the left subclavian artery, about half its normal diameter between this point and the constriction, and of about normal size below the constriction. The innominate and both subclavian arteries were dilated, the subclavian being about twice the diameter of the carotids. The upper three pairs of intercostal arteries arising from the aorta beyond the constriction were much enlarged, especially the upper pair. The external iliac arteries were much larger than the internal, and the deep epigastric arteries were enlarged. The femoral arteries were of normal size. There was no abnormality of the cardiac valves or septa. The pulmonary artery and its branches were normal.

The mode of origin of this type of stenosis is uncertain. It has been ascribed to kinking of the aorta by contraction after birth of a long ductus arteriosus or to an extension of the peculiar tissue of the ductus arteriosus into the aortic wall. West thinks it probable that in the adult type the condition arises after birth so that the gradual increase of pressure in the aorta above the constriction leads to dilatation of the arteries forming the collateral circulation, which, as in the present case, may be so efficient that there are no symptoms and life is not shortened. In the majority of cases symptoms have appeared somewhat late in life. In some they have been present throughout life. The symptoms include headache, vertigo, buzzing in the ears, lividity or suffusion of the head and neck, and thoracic or abdominal pain; cardiac insufficiency frequently supervenes and produces symptoms. The physical signs are similar to those of the present case, being chiefly those due to the collateral circulation, and especially greatly increased pulsation in the neck and upper limbs, but not in the lower limbs. Death in many cases has occurred suddenly, rupture of the heart or aorta being found. In a large proportion death follows a stage of broken compensation. In a certain number, of which West's case is an example, the condition does not interfere with the duration of life, death being due to an intercurrent complaint.

A case of stenosis of the aortic isthmus is described by Lommel of the Jena Medical Polyclinic in a woman aged 38, associated with funnel chest, which he thinks may have been a factor in its causation. According to Barié 37 per cent. of his cases showed congenital malformations of the heart or other organs. Pulsation of the collateral arteries, which is a valuable diagnostic sign and was well marked in both West's and Lommel's patients, occurs, according to Vierordt, in only about a quarter of the cases, so that not infrequently the condition is not discovered until the autopsy.

Rupture of the aorta. The recent paper by Oppenheim (vide *Medical Supplement*, 1919, **2,** 82 *a*) induced Binder to record a case of spontaneous rupture of the ascending aorta in a soldier aged 20 which occurred after a severe physical effort. The autopsy, as in one of Oppenheim's cases, showed coarctation of the aortic isthmus, corresponding to Bonnet's adult type of stenosis and a somewhat hypoplastic state of the rest of the aorta. The rupture occurred at the usual site, a little above the valves. The rise of blood-pressure necessitated by the stenosis had led to sclerotic changes in the vessel wall which were most pronounced in the arch of the aorta and at the sites of origin of the large vessels, while the ascending portion on naked eye examination showed only slight changes. Even the microscopical lesions in the ascending aorta were not sufficient to explain the rupture, although the elastic fibres of the media had partly disappeared. Cases of this kind prove that a spontaneous rupture of the aorta does occur, and that a rise of blood-pressure through indirect trauma in the widest sense of the term leads to rupture at the functionally weakest part without a change in the vessel wall being necessary.

According to Löffler of the Bâle Medical Clinique the great majority of cases of rupture of the aorta in young persons apart from mesaortitis occur in association with well-marked hypertrophy of the left ventricle, such as is most likely to be found in chronic nephritis. The terminal stage of chronic nephritis with convulsions and subsequent still further rise of blood-pressure seems specially to predispose to rupture of the aorta. It is not always, however, the convulsive form of uraemia in which a rupture of the aorta is found. Löffler recently reported two cases of chronic uraemia in a woman aged 38 and a man aged 40 who both died of rupture of the aorta, although they had never had any convulsions and had both been confined to bed during the last week of their lives. Macroscopically the aortic wall showed distinct changes which consisted in diffuse thickening of the intima with localized areas in which the thickening was more pronounced, but were nowhere very severe. The Wassermann reaction was negative in both cases. These cases are of interest because they show that with a high blood-pressure spontaneous rupture of the aorta may occur without there being any obvious cause, a fact which is of considerable forensic importance. The classical site for the rupture is just above the attachment of the sigmoid valves, the course of the tear is usually transverse and involves only one part of the circumference of the aorta.

Löffler now records another case of spontaneous rupture of the aorta in chronic nephritis in a woman aged 38, whose blood-pressure had ranged between 175 and 210 mm. Hg with Riva-Rocci's instrument. The autopsy showed contracted kidneys, excentric cardiac hypertrophy, slight fibrous myocarditis, multiple ruptures of the aorta, dissecting aneurysm of the ascending and descending aorta and haemopericardium. Of special interest was the fact that microscopically no remarkably severe lesion could be found at the site of the rupture. The intima, it is true, was thickened and showed droplets of fat and finely granular calcification, but no lymphocytic infiltration was found in the media. The elastic fibres had a quite normal appearance. Although the aortic wall could not be regarded as normal, the changes were not sufficient to account for its rupture, the chief cause of which was the high blood-pressure associated with a hypertrophied and powerfully acting heart.

A similar case is reported by Feliu in a man aged 40. The patient had no history of venereal disease, but was suffering from chronic nephritis and myocarditis. The maximum blood-pressure was 17 and the minimum 11 with Pachon's oscillometer. The patient suddenly felt a severe pain in the left side, became cyanotic and died in half an hour. At the autopsy, in addition to the renal lesions and signs of chronic pulmonary tuberculosis, a transverse rupture of the aorta was found. The aorta did not present any atheromatous or other lesion than the tear which was situated immediately above the insertion of the sigmoid valves. The heart, and especially the left ventricle, was hypertrophied. Microscopical examination of the aorta merely showed a degeneration of the intima and part of the media in the neighbourhood of the rupture.

According to Sternberg, who reports two examples, 60 cases of perforation of an aortic aneurysm into the pulmonary artery are on record, about half of which have been observed during life, while the rest died shortly after occurrence of the perforation. In the first of Sternberg's cases, a man aged 45 whose history could not be obtained, there was an aneurysm in the anterior wall of the aorta just above the valves, which is the typical site for this rupture to occur, as this is the only place where aneurysms can project into the pulmonary artery. The second case, in which there were two perforations in the anterior wall of the aorta opening directly into the pulmonary artery, was not really an example of a perforation of an aneurysm but a rupture of part of the aorta, all the layers of which were atheromatous. The patient survived for some time as was shown by the smooth edges of the perforation. Fifteen weeks appear to have elapsed between the first and second perforation, and even after the second life was prolonged for a few weeks more.

Menetrier and Durand report a case of rupture of the aorta in a syphilitic woman aged 43 who died 48 hours after the onset of the symptoms. The rupture was found 2 cm. above the sigmoid valves on the posterior surface of the vessel, where the aorta presented a dissecting aneurysm. Histological examination showed a mucoid degeneration of the connective tissue of the media.

According to Herrick rupture of an aneurysm of the aorta into the superior vena cava is a rare event. Pepper and Griffith in 1890 found only 29 cases on record. Fussell in 1906 was able to add 7 more. The case reported by Herrick with 6 others found by him in the literature since 1906 makes a list of 43. The diagnosis is made by the sudden onset of the symptoms, especially cyanosis, oedema, coldness, and distension of the veins of the upper part of the body with other evidence of obstruction to the circulation of the blood in the tributaries of the superior vena cava. If there is no obstruction below the point of entrance to the azygos vein, oedema of the chest wall will be absent, and there will be less likelihood of marked hydrothorax. A murmur which is usually continuous is heard towards the base of the heart with a ventricular systolic crescendo. In Herrick's case, which occurred in a man aged 33, the rupture took place into the left innominate vein less than 1 cm. from the superior vena cava. The autopsy showed typically syphilitic aortitis.

Aneurysm of the abdominal aorta has been rarely diagnosed during life, probably owing to its relatively infrequent occurrence. Schroetter states that only 3 cases were seen in the course of 10 years among 19,300 necropsies at the Vienna Institute of Morbid Anatomy. In 1902 Philip was able to collect 92 cases from literature, in only a few of which the diagnosis had been made during life. According to Böttner only 3 cases have hitherto been diagnosed by X-rays. Högler, from whose paper the above information has been taken, records a case in a woman aged 61 in whom the diagnosis of aneurysm of the abdominal aorta in the region of the coeliac axis with areas of calcification in its wall was made by X-ray examination. The following symptoms indicated the localization of the aneurysm: (1) cachexia with the preservation of a good appetite, (2) the character of the pain, (*a*) the occurrence of deep-seated abdominal pain with neuralgic attacks on change of position as well as on defaecation and physical effort. (*b*) propagation of the pain to the intestinal canal simulating colic. The issue of the case is not recorded.

Arterio-venous aneurysms are more common as a result of the war. They produce a continuous murmur with systolic accentuation, whereas the narrowing of a large artery is indicated by a systolic murmur. Several authors have reported that slowing of the pulse and increase of blood-pressure result from manual compression of the aneurysm, but their explanations of this phenomenon are various. Frey considers that a stimulus at the site of pressure is conveyed to the vagus and vasomotor centres thereby reflexly inducing the bradycardia and rise in blood-pressure. Incidentally he noted that the overfilling of the venous system, inseparable from the aneurysm, produced distinct enlargement of the heart with an apical systolic murmur and an accentuated pulmonary second sound. These signs disappeared completely ten days after the curative operation.

According to Gallavardin and Contamin in the majority of cases of **arterial occlusion** of embolic origin it is not the embolus which is dangerous but the thrombotic process arising therefrom. They record examples of embolic gangrene in which the onset was gradual and progressive, a circumstance which they attribute to the fact that the arteriole which is first occluded by the embolus is of minute size so that no symptoms occur before the development of ascending thrombosis. In some cases of gangrene of both lower limbs the condition is due not to a second embolus from the heart but to the detachment of a clot from the side first affected and its passage to the bifurcation of the abdominal aorta. The practical interest of such cases is that expectant treatment should not be too prolonged but that amputation should be performed as soon as it appears impossible that spontaneous recovery can take place.

Many writers on **sphygmomanometry** have noticed that the results vary with successive readings. It has been stated that the fall which is observed when estimations are made for several minutes is merely due to disappearance of the preliminary excitement of the patient. Tixier shows that it still occurs when individuals are accustomed to the procedure. He gives the figures obtained in a large series of subjects, normal and abnormal, by successive readings with the auscultatory method. Extraneous causes such as slight movements, cold, noise, and even undue interest shown by the patient may alter the pressure, and these were carefully excluded. It is rare to find the figure stationary with these precautions. The most usual formula is a steady slight decrease in the systolic blood-pressure, with little or no decrease in the diastolic, during the first few minutes. After this time the residual or terminal pressure may remain fixed, though even this may show slight periodic undulations perhaps comparable with Traube-Hering curves. The author describes cases exhibiting the less frequent variations, such as those in which the arterial pressure does remain fixed, those with an excessive fall in systolic pressure, and those rare cases with an increased pressure accompanied by noticeable general distress. Several patients with cardio-renal symptoms and signs provided examples of a progressive increase in diastolic pressure during repeated observations.

The pulse-rate had no clear relation to the variations under discussion. Though not admitting the hypothesis of active systole of the arteries, the author argues that the modifications observed are due to a local vasomotor change in the arm caused by repeated compression of the brachial artery. The practice of prolonged readings over several minutes provides in some measure a functional vasomotor test and gives some index of the condition of the peri-arterial sympathetic system. Thus are distinguished; (1) *normals* with slight systolic fall and diastolic fixity, as described also by Gallavardin, (2) *tensostats* with no variations, depending on vagotonia, slight arterial change, or lack of sympathetic excitability, and (3) *tensolabiles* with a hyperexcitable heart or sympathetic vasomotor system. It is therefore recommended that a complete blood-pressure examination should include not merely the initial reading and the terminal or residual reading, but also the whole reaction of the individual to successive estimations during several minutes.

Postural changes in the blood-pressures. From observations on several hundreds of subjects Sewall has come to the conclusion that in changing from the recumbent to the standing posture there is always a rise in diastolic pressure, and a fall in pulse-pressure, and that in normal (and some pathological) cases the systolic pressure does not change materially or shows a rise. Excessive fall of systolic blood-pressure in the erect posture indicates weakness of vasomotor control, while excessive rise of diastolic pressure denotes vascular spasm and abnormal effort. Each results in abnormal depression of pulse-pressure, the maintenance of which at a certain height is necessary for the proper nutrition of the brain and other tissues. The blood stasis manifested by fall of systolic pressure can be counteracted by the support of an abdominal belt, and small doses of digitalis are indicated when there is an abnormal rise of the diastolic pressure. Comparatively few of Sewall's cases showed organic disease of the heart, arteries, or kidneys, and the manifestations of chronic circulatory deficiency were probably due as a rule to toxaemia from focal infection or to occult tuberculosis.

Sewall points out that the maximum arterial blood-pressure is more or less markedly affected by respiratory movement, being highest during expiration and lowest during inspiration. The difference between the maxima taken in the two phases of respiration may vary with quiet breathing from 0 to 20 mm. The systolic pressure is also subject to another secondary cause of fluctuation which probably consists in more or less slow variations in the intensity of the vasomotor tone, the height of maximal pressure apparently changing 30 mm. Hg within a minute from this cause.

Kahn, assistant at the cardiographic laboratory of Mount Sinai Hospital, New York, has studied the effect of raising the arm upon auscultatory blood-pressure readings in normal cases, neurocirculatory asthenia, thyrotoxic conditions, tachycardia, nephritic hypertension and endocarditis. The normal effect was a progressive fall of the systolic and diastolic blood-pressure readings as the arm was raised upwards, the amount of fall increasing with the elevation. The fall of pressures was more marked than normal in cases of neurocirculatory asthenia, and was most perceptible in cases of hyperthyroidism and exophthalmic goitre. In nephritic hypertension the readings remained high in spite of elevation of the arm. In aortic regurgitation the diastolic pressure fell more steeply than the systolic, and its main reduction occurred up to 90 degrees elevation.

Blood-pressure in childhood. Mosler and Herzfeld of the 3rd Medical

Clinique of Berlin University investigated the systolic blood-pressure of 150 children aged from 5–14 years with the Tycos apparatus and found that the average readings were as follows; 4–5 years 84–82 mm. Hg, 6–9, 91–86 mm., 10–12, 102–93 mm., 13–14, 110–109 mm.

Riesman of Philadelphia describes a form of **hypertension in women** characterized by the following features: (1) The patients are usually stout and undersized. (2) They have borne many children. (3) They have neither a history nor any stigmata of syphilis. (4) They are over 45 years of age. (5) They are practically all constipated. (6) They show an amazing tolerance for high pressures up to a certain degree. The average systolic tension in Riesman's patients was 211, the average diastolic pressure 105, the highest systolic pressure 310, and the highest diastolic pressure 160. (7) In most cases the heart is enlarged, especially to the left. (8) The arteries are soft, and even the retinal vessels show no involvement. (9) The kidneys are competent. The principal factors in the condition appear to be (1) multiple gestations, (2) worry, (3) constipation and intestinal indigestion, (4) the menopause. The symptoms are dizziness, ringing in the ears, anginoid pains, palpitation, gaseous distension and vasomotor disturbance. A systolic murmur at the aortic area and a ringing second aortic sound are common. In the later stages a soft systolic murmur can often be heard at the apex. The prognosis is on the whole favourable, but three important complications may occur, viz., (1) angina pectoris, (2) apoplexy with hemiplegia, (3) decompensation, a late stage of the disease arising from myocardial exhaustion.

In an article on **trauma and arteriosclerosis** Fraenkel of the Pathological Institute of Hamburg University records a case of localized arteriosclerosis of the abdominal aorta in a soldier aged 29 who died 18 months after a gunshot wound which caused softening of the lower dorsal cord. The fact that localized arteriosclerosis following trauma has not been more frequent in the course of the war is attributed by Fraenkel to the majority of the cases proving fatal much sooner, whereas the present patient survived one and a half years. A severe injury to the vessel wall is not necessary, but only a sort of molecular concussion, as the result of which, as in Fraenkel's case, a dissociation takes place in the elastic and muscular fibres of the media. While admitting a causal connexion between the trauma and localized arteriosclerosis, Fraenkel agrees with Finkelnburg and Reinhardt in absolutely denying any connexion between general arteriosclerosis and a previous injury, and not only regards the development of sclerosis of the cerebral arteries after cephalic trauma as unproven, but is also sceptical as to the possibility of aggravation of pre-existing cerebral arteriosclerosis by an injury of this kind.

During a recent outbreak in Vienna of a disease resembling osteomalacia Arnstein and Schlesinger treated several cases with subcutaneous injections of adrenalin and found that elderly patients showed such severe or unusual reactions that they decided to study the effects of adrenalin in non-osteomalacic cases. The investigation was carried out on 50 patients, 39 of whom were above 60 years of age. Both sexes were equally represented. The results were as follows: after subcutaneous injection of 0·3–0·8 mg. of adrenalin a fall of blood-pressure, occasionally preceded by a rise lasting a few minutes, took place and continued for some hours, or else the blood-pressure remained unaffected without any change in the pulse-rate or with a bradycardia of some hours' duration. The latter, however, did not run parallel with the fall of blood-pressure. In many instances the fall of blood-pressure was due to cardiac failure, in which case tachycardia was present. In other cases the fall of blood-pressure was attributed by the writers to stimulation of the vasodilators by adrenalin, and the calcium deficiency of the organism. After injection of adrenalin old persons often had bradycardia lasting for several hours even though there was no associated fall of blood-pressure, but sometimes the pulse-rate was not affected, possibly owing to a change in the mode of reaction of the vasomotor nerves. The occurrence of anginal attacks after injection of adrenalin only took place when there was atheroma of the coronary arteries. After injection of moderate doses (0·3–0·8 mg.) glycosuria was exceptional, being found in only 10 per cent. of the cases.

Wiesel and Löwy of the Francis Joseph Hospital in Vienna remark that every one familiar with the symptoms of disease of the circulation knows how frequently the clinical picture is not explained by the post-mortem findings. At the autopsy on cases of very severe circulatory insufficiency which are little or not at all affected by treatment, the heart is found to be in a good state of preservation, and even on histological examination no essential disease is found. Examination of the aorta and large vessels, as well as of the kidneys, shows nothing abnormal apart from congestion. On the other hand, it not infrequently happens that post-mortem examination of elderly persons who have died of some intercurrent disease shows that the heart muscle is extraordinarily atrophic, although they had shown no signs of cardiac disease during life. In an endeavour to account for these discrepancies the writers during the last two years have made a careful examination of the peripheral vascular system in cases of acute and chronic cardio-vascular disease. The arteries of the viscera as well as those of the brain and extremities up to the size of the digital arteries were examined. Definite lesions were found in the vessels in every case of chronic circulatory failure and also in renal disease accompanied by oedema and in valvular disease even when no signs of chronic insufficiency were present. The lesions were confined to the media and were quite distinct from those of arteriosclerosis with which they were occasionally associated. The affection commenced with an oedema of the vessel wall, a serous infiltration of the media taking place. As the result of compression by the oedema the muscle fibres became atrophied and the nuclei more or less completely disappeared. Finally cicatricial tissue was formed and occasionally calcification took place, but the calcareous deposit was always in the media. The lesions were not confined to old persons, but occurred at all ages, being found in children as young as 18 months, and were quite as frequent as arteriosclerosis. Aetiologically toxi-infective processes were responsible, especially in the vasa vasorum.

Stoerk and Epstein, commenting on Wiesel and Löwy's paper, stated that they had made similar post-mortem observations on the vessels of persons aged between 13 and 23 who had died of influenza. The peripheral arteries showed severe lesions consisting of necrotic changes chiefly affecting the elastic and contractile elements. Though the lesions were chiefly found in the media and elastic layer, the sub-endothelial layer was also affected. In every case the whole arterial system was involved with the exception of the cerebral vessels and branches of the pulmonary artery. The presence of these severe lesions, which chiefly affected the contractile and elastic elements of the vessel wall, accounted for the gravity of the circulatory symptoms in influenza and explained why no benefit was derived in such cases from the use of cardiac stimulants.

Clinical cardiography. As a result of the observations recorded in great detail in his paper, Kilgore concludes that there are respiratory variations of heart-rate even in the presence of auricular fibrillation. This arrhythmia is to all appearance so absolute that the superimposition of such respiratory variation, obvious with a normal sinus rhythm, could only be demonstrated by the analysis of a very large collection of combined radial and respiratory tracings. The average figures collected and the resultant diagrams to show the respiratory effect in nine cases do not all support the author's claim, but many of them suggest a respiratory effect. It is not so simple a variation as that in respiratory sinus arrhythmia, where there is acceleration of rate during inspiration and retardation during expiration. In auricular fibrillation it could be explained by neurogenic fluctuations in bundle conductivity or in the rate of recovery of ventricular excitability, or both.

It is known that the heart tends to beat less frequently during sleep. Klewitz has compared the electrocardiograms of waking hours with those from the same subjects during sleep. He finds that there is not merely a lengthened diastole, as would be expected, but that the systolic period both auricular and ventricular is prolonged during sleep. The *P–R* interval, an index of conduction time, is also increased. Tables show the numerical results in healthy individuals and in patients with valvular and other forms of heart disease. The significance of the change is discussed. The form of the electrocardiogram was often greatly modified, but this may depend on the adoption of a change of position while asleep.

The proximity of the left auricle to the oesophagus allows the registration of the auricular movements by means of a hollow oesophageal sound with an elastic receiver at the lower end and some form of registering apparatus connected with the upper. Weitz and Schall have extended previous observations in recording the movements by the sensitive photographic method of Frank and combining with them synchronous electrocardiograms for comparison and guidance. The curves display rather more detail than jugulo-carotid tracings and have the advantage of recording the heart sounds and, under favourable conditions, murmurs. Normal oesophageal cardiograms and their common variations are reproduced and discussed, and then those obtained from patients with valvular disease and the various common irregularities.

Boden summarizes the results of section and stimulation of the vagi and sympathetic nerves upon the form of the electrocardiogram as seen in animal experiments by Einthoven and subsequent workers. The observations of Weil on the human electrocardiogram as modified by vagal pressure are also quoted. The author describes the influence of the vagus in a youth with paroxysmal tachycardia. The abnormal form of the electrical curve during the attacks was identical with that produced by an injection of atropin. Failure of the normal negative chronotropic vagus action is suggested as the immediate cause of the paroxysms.

The effect of vagal pressure upon the healthy human heart is of great physiological interest, and coincides to a great extent with that observed in animal experiments. It has long been known that the right vagus influences especially the sinus node (rate), and the left vagus the A-V node (conduction). Kleemann investigated these effects of pressure in the neck, right and left, upon 150 subjects. Some were healthy, some the subjects of various heart diseases. Electrocardiographic records were used and many valuable ones are reproduced. It is true that the right vagus specially influences the sinus node, but it can also control the A-V node. the centres in the ventricle, and the A-V bundle. Similarly the left vagus can influence the sinus node as well as the other centres.

The individual reaction to vagal pressure varies enormously. The majority are uninfluenced. A large number follow the rule. Yet many unusual effects are encountered, such as the following. Complete standstill of the heart for as long as 10–15 seconds was recorded. A normal positive P wave became negative in two cases during pressure on the right vagus. The left vagus induced premature contractions in a few cases. The ventricular rate in auricular fibrillation was reduced especially by the right vagus; this is ascribed to depression, not only of conduction but also of the excitability of the ventricle. A striking effect of vagus pressure in temporarily abolishing partial heart-block is recorded. Vagal control of the sinus node becomes manifest earlier than that of the bundle.

The author agrees with Wenckebach and with Weil that patients with heart disease are generally more susceptible than healthy subjects. But the effect observed bears no relation to the degree of myocardial failure, and is not yet of value in prognosis.

Weber recognizes that the only fundamental change in the venous pulse of auricular fibrillation is the absence of the auricular (*a*) wave. Yet he finds that five different types may be separated if sufficient tracings from different patients are examined. Illustrative photographic records including electrocardiograms are given. The time relations of the venous waves as described by English writers are questioned. Instead of the systolic collapse occurring *during* systole and the diastolic at the end of systole, he maintains that the systolic collapse (the first negative wave) occurs at the end of systole, and the diastolic collapse (second negative wave) about $\frac{1}{10}$th second later. The systolic collapse is due to retraction of the still closed tricuspid valve by the papillary muscles, and much more to the lowered intrathoracic pressure caused by the sudden extrusion of the ventricular content from the thorax.

In conditions of venous stasis the systolic collapse will be slighter and the diastolic wave earlier because the fall in intrathoracic pressure is more rapidly stabilized from the congested veins. In type 3, by far the commonest of the five types in fibrillation, this results in fusion of the systolic and diastolic waves in a single plateau with merely a dip about the middle, a rudimentary systolic collapse. Another feature in extreme stasis is exaggeration of the diastolic collapse or second negative wave. This is not only relative because of the slighter systolic collapse, but actual as the veins are tense and the curve equable except only when the enlarged right ventricle itself fills (type 5).

In a patient with a wound of the chest the resulting cavity chanced to lay bare the right auricle. Straub improvised a form of plethysmograph to register its changes in volume and took synchronous tracings from the jugular vein and carotid artery. The records thus obtained are discussed in relation to current interpretations of the several waves obtained in jugulo-carotid tracings. He confirms the view that the '*v*' wave can begin during ventricular systole and that it ends as the auriculo-ventricular valves open. It is due to stasis before the closed valves, and will therefore begin earlier in the heart's cycle when blood has collected in the venous reservoir as during heart failure.

According to Laubry and Mougeot a useful pneumograph can be made by taking the part of a cycle tyre inner tube which carries the valve and fixing it within a simple belt to fit lightly round the chest. With this apparatus connected to one of the tambours of Mougeot's polygraph, the authors investigated periodic sinus arrhythmias. They found that in children this could almost always be demonstrated by measurement of successive pulse periods when it was not obvious to palpation. Graphic records are reproduced showing special varieties of sinus arrhythmia, including periodic single pauses, sporadic premature contractions at the end of expiration, and phasic variations independent of respiration.

Laubry and Mougeot subsequently deal with the less understood anomalies in the amplitude of the pulse, of respiratory origin. Diminished amplitude during inspiration, which is the common physiological finding, is accentuated not only in adherent pericardium, but also by compression of the subclavian artery in forced inspiration from any cause. Thus it is found with laryngeal stenosis and with large pleural effusion, even to the extent of disappearance of the pulse during inspiration (pulsus paradoxus). Additional factors may be the augmented intrathoracic pressure, and also vagotonic diminution of ventricular contractility, for it may disappear under atropin. Tracings are given showing an inverse type with depressed amplitude of the pulse during expiration.

Schutz has demonstrated that in patients with meteorism the enlargement of the heart, especially to the right, seen on orthodiagraphic examination in the erect posture, appears less when they are examined horizontally. Porges confirms this fact and agrees that the enlargement should not be lightly ascribed to a 'fatty heart', for it may be reduced without any loss in body weight. He tabulates the findings in patients before and after treatment of the abdominal distension by diet and saline purges. The cause of the phenomenon is displacement of the heart forward against the anterior chest wall by increased tension of the diaphragm, and to a less extent by its higher position. After treatment the heart lies lower and the cardio-hepatic angle becomes smaller.

Treatment. Pfalz treated various forms of cardiac disease with intravenous injections of a 12–20 per cent. solution of glucose. On the average 6–10 injections were given in doses of 200–300 c.c. at weekly intervals. The best results were obtained in two cases of sclerosis of the coronary arteries with angina pectoris and high blood-pressure, in which at the end of treatment the anginal pain had almost entirely disappeared. In three cases of general arteriosclerosis with high blood-pressure and angina pectoris, and in a case of peripheral arteriosclerosis and syphilitic aortitis with angina pectoris the anginal attacks were diminished and the physical capacity improved. In a case of myocardial degeneration with auricular flutter and cardiac insufficiency considerable improvement also took place in the subjective symptoms and cardiac condition, the heart sounds becoming more distinct and the accidental murmurs disappearing.

Volkmann of Brunswick, who has had two successful cases, recommends the following technique for intracardial injection. A needle 4 cm. long is passed through the fourth left intercostal space in the angle formed by the sternum and the fourth and fifth ribs along the border of the sternum rapidly down to the heart. The pericardium usually cannot be felt. The needle is then driven 1 cm. deeper and so reaches the cavity of the right ventricle. The internal mammary and intercostal vessels and the vagus are avoided by this method. Injection into the heart muscle as recommended by von der Velden (vide *Medical Science*, 1919, **1**, 80), should be avoided owing to the damage caused to the tissue, even if only 1 c.c. is injected. 20 c.c. of a 1 in 1,000 solution of suprarenin and normal saline is then injected in the course of two minutes. In three minutes' time the effect of the injection becomes perceptible, and an attempt should then be made to keep the circulation going by continuing the injections. Large quantities of fluid need only be given in exsanguinated patients, smaller doses being used in other conditions such as valvular disease, acute infections, anaesthetic accidents, asphyxia, poisoning, &c.

Hare has treated 30 cases of aortic aneurysm by the introduction of gold platinum wire and electrolysis, thereby causing an extraordinary decrease in pain and an arrest of progress of the growth. The following conditions are necessary for success: (1) the aneurysm must be sacculated, not fusiform; (2) it must be near enough to the chest wall to allow the insulated needle to enter the sac; (3) the amount of wire varies with the size of the sac, but is usually from 15–20 feet; (4) the time during which the current is allowed to pass is usually about 45 minutes, and the current strength must be turned on and off very gradually.

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TUBERCULOSIS

Epidemiology. In an article on tuberculosis among the European nations at war, Miller divides the civilian population of Europe into two main groups: France and England on the one hand, and Belgium, Germany, and Austria on the other. In the former, tuberculosis has only slightly increased since the war, the increase being mainly among young women in industry; in the latter all classes of the community have suffered, and to a rapidly increasing extent as war went on. The principal difference appears to be that of food. Speaking generally, the civilian population in France and England has not suffered from insufficient nourishment, whereas in the other group of countries there has been long-continued under-nourishment among the masses of the people, and the increasing mortality from tuberculosis has undoubtedly been largely due to this factor. So striking has been the effect of partial starvation on tuberculosis among all classes that Addams and Hamilton during a visit to Germany after peace had been signed were informed by Kayserling that German physicians were beginning to maintain that tuberculosis should be regarded primarily not as an infectious disease, but as a disease of nutrition to be controlled much more by feeding than by preventing infection. Miller states that little information is available as to conditions in Serbia, Russia, Poland, Armenia, and Roumania, but there is every indication that there has been an enormous increase in tuberculosis in these countries as the result of privation and insufficient food.

In 1909 the Finnish Association for Combating Tuberculosis selected the parish of Kronoby in the north-west of Finland for a wholesale examination of the population for tuberculosis, and for the institution of a campaign against this disease, with the dispensary as the central organization. The features of this campaign were instruction in general hygiene, tracing sources of infection and eliminating them as far as possible, early diagnosis and treatment. But the principal object of the campaign was protection of children from infection, and provision for their general welfare. Ten years later, Tennberg, who carried out the wholesale examination for tuberculosis in 1909, covered the same ground with a view to finding out the effects, if any, of this campaign. In 1909 pulmonary tuberculosis was found in 28·31 per cent. of the families examined. The corresponding figure in 1919 was only 14·56 per cent. The proportion of cases of pulmonary tuberculosis among the examined (3,148 in 1909, and 3,272 in 1919) was reduced from 6·20 to 2·83 per cent. In 1909 it was found that the morbidity was highest between the ages 11 and 20. After 20 it slowly fell, but rose again in old age. In 1919 the decrease in the morbidity was greatest between the ages 11 and 20, being from 8·86 to 2·63 per cent, Tennberg points out that the comparatively great decrease in the morbidity rate early in life is particularly significant, as indicating the ability of a child-welfare campaign to reduce the tuberculosis morbidity. Among the 89 cases of pulmonary tuberculosis found in 1919, the disease was active in 55, inactive in 34. The morbidity was as high at the age of 71 to 80, as it was at the age 31 to 40. A comparison of the incidence of enlarged cervical glands in children under 15, showed a fall from 40·90 to 29·77 per cent., and in the total population of all ages, from 16·50 to 12·10 per cent. An unknown proportion of these cases of adenitis was, however, non-tuberculous.

Aetiology. For the purpose of discovering whether infection in guinea-pigs followed exposure to what may be considered to be sufficient exposure for infection of man, Brown, Petroff and Pasquera carried out experiments which showed that the danger of dust of rooms, from telephone receivers, the danger from properly cleansed eating utensils, and the danger from hands infected by hand-shaking or from door-knobs were not confirmed, whereas the danger of transmission of tubercle bacilli to eating utensils and thence if not cleaned to a second person was borne out.

Alcoholism and Tuberculosis. Mouisset states that the relatively small number of cases of tuberculosis among prisoners repatriated from Germany was one of the few agreeable surprises of the war. Two series of statistics, each drawn up from 15,000 repatriated prisoners, estimate the number of tuberculosis cases at 14 per cent., and of these only 3·5 per cent. were severe cases. The numerous deaths which occurred among prisoners in Germany were due to acute disease. Much as the men had suffered during their imprisonment, they had not been able to indulge in alcohol to excess, so that their involuntary sobriety was a circumstance in their favour.

Koelsch publishes a long and very complete study of the Bavarian porcelain industry, which should be seen in the original by those who are concerned with **industrial lung affections.** In the past the statistics relating to the incidence of dust disease and of tuberculosis in this class of worker have been rather confused, and this the author ascribes to a lack of clearness in separating off statistically those workers who are engaged in the by-occupations of the trade, and those who are actually subjected to the dangers inherent in it. It is impossible here to follow out the technicalities of the different groups, but putting together in one class those who actually worked in the dusty processes, Koelsch found that their tuberculosis death-rate was about three times that of the rest of the population in the same district. This increased liability he ascribes for the greater part to the direct influence of pneumokoniosis on the respiratory tract itself, while not denying an influence to certain other industrial conditions, which vary from place to place. So far as this industrial tuberculosis is concerned, he is of opinion that adult re-infection is of more importance than infection in childhood. A list of essential precautionary measures with regard to work-rooms, dust-disposal, clothing, and hours of work is given, for which the paper should be consulted.

The author made a personal clinical study of 1,000 porcelain workers of both sexes, actually engaged in the industry at the time of examination. He found 3 per cent. to be suffering from acute or chronic bronchitis, and 2 per cent. to be suffering from pulmonary tuberculosis. But of the total number examined pneumokoniosis was diagnosed in nearly 50 per cent. from the clinical examination. Subjective symptoms were few, slight shortness of breath, dryness in the throat, or pain in the chest on deep breathing. Few had coughs or sputum. Percussion showed some dullness at the apices or in the interscapular space; but auscultation was more valuable, and rough vesicular breathing with prolonged expiration was a constant finding. More than half of a series of cases which were X-rayed showed positive findings ascribed to pneumokoniosis, namely in early cases a more or less characteristic hilus shadow and later bilateral granular shadows tending to fuse into masses as the condition progressed. The various dust components involved are thoroughly described and illustrated, and the relative importance of kaolin, quartz, and felspar discussed. The author emphasizes the fact that even dusts which do not appear morphologically dangerous, and are entirely insoluble, can still evoke tissue reaction if present in sufficient quantity.

War and tuberculosis. In 1917 Zadek, director of the tuberculosis sanatorium at Neukölln, found from study of 300 cases of tuberculosis in soldiers, that the numerous attacks which developed during military service were mainly due to a recent infection, and showed a progressive character, whereas, among those who had formerly had lung trouble and had subsequently developed tuberculosis again during military service, there was not such a tendency to a malignant course. Examination of another 300 cases in the same sanatorium confirmed his previous observations. Zadek concludes that primary attacks of tuberculosis are frequent in war time, and of unfavourable prognosis, whereas, in exacerbations of pre-existing disease the outlook was better. These facts support the view maintained by Römer and Much, that an early infection with tuberculosis in childhood appears to have a more favourable prognosis than a later infection in adult life. In this connexion, considerable interest attaches to the observations of Teleky who found that the tuberculosis incidence and mortality among country people who had moved into towns was considerably higher than that of the native population.

In an article on the mortality from tuberculosis during the war, Gruber shows that the mortality from tuberculosis per 1,000 inhabitants in the town of Mayence fell from 4·21 in 1904 to 2·18 in 1914, since when it has risen to 4·30 in 1918. On the other hand, in the country district round Mayence the tuberculosis mortality was 2·41 per 1,000 in 1905, 1·50 in 1915, and 2·30 in 1917, the difference in mortality being due to the unfavourable conditions of town life, especially in war time. During the last 15 months of the war Gruber found that 25 per cent. of the deaths among civilians in Mayence were due to tuberculosis, and that another 10 per cent. had had latent tuberculosis. The number of deaths from tuberculosis in Mayence. which is not an industrial town, was thus higher than in the industrial town of Dusseldorf in which the figure was 22·7 per cent. in peace time (Lubarsch).

Jacob deals with his experiences of pulmonary disease near the front in Flanders. Like others, he was surprised at the comparatively small incidence of respiratory affections as a whole. They formed only 13 per cent. of the total visceral disease, as against 35 per cent. in peace time. These figures are not directly concerned of course with lung wounds, but the author remarks that he saw few complaints following relapse of chest wounds among men who had been able to return to the front line. Of the cases reported, all but about 7 per cent. were admitted for symptoms pointing to a lung infection.

Tuberculosis in its various forms naturally heads the list. Some of the open cases held on to active service with remarkable tenacity. They averaged nearly 11 months before reporting sick. It is diagnostically rather disturbing to find that the author gives three groups, namely, active closed tuberculosis, probably active tuberculosis, and inactive tuberculosis, each of which contains approximately double the number of his open cases; but it is fair to record that he was amazed at the comparative scarcity of tuberculosis of severe course during the rigors of the first winter of the war, considering the number of soldiers who gave a history of pleurisy, haemoptysis or apical catarrhs. Out of 340 typhoid cases, about a third of which were severe, only twice was a latent tuberculosis brought into evidence. Moreover, the general impression in the field seems to have been that recent tubercle was not a common intercurrent finding in general autopsies. Those cases of tuberculosis of acute course which became specially labelled 'war tuberculosis', were for the most part tuberculosis occurring in robust, previously healthy subjects.

The question of deciding on a man's capacity for active service is still far from solved, but Jacob implies that in a war of position, sufficiently stationary to permit good medical observation in and behind the trenches, it is not necessary to be too drastic in one's attitude towards the suspicious candidate for field service.

Wounds of the lung and pulmonary tuberculosis. In 27 cases of wounds of the chest studied by Tecon and Lausanne among the soldiers of the allied armies interned in Switzerland only 5 or 18·5 per cent. showed pulmonary tuberculosis with tubercle bacilli in the sputum, but in only 2 of these, or in 7·4 per cent., could a causal relationship be established between the chest wound and pulmonary tuberculosis. In several instances it was observed that a penetrating wound of the chest did not exercise any localizing influence on the tubercle bacillus.

Tecon emphasizes the fact that all the cases had been specially selected, having been sent to him as a specialist in diseases of the respiratory system with the diagnosis of tuberculosis. Moreover, all the patients had undergone a long term of imprisonment which is specially favourable for the development of tuberculosis, as the disease is very prevalent in prison camps. Under these circumstances, therefore, the frequency of tuberculosis following chest wounds is not likely to have been under-estimated. With the object of seeing if his conclusions as to the rarity of post-traumatic tuberculosis were verified by the study of fresh material, Tecon examined 1,033 cases of pulmonary tuberculosis interned at the Leysin Sanatorium and found only 53, or 5·1 per cent., with chest wounds, and of these only 12, or 1·1 per cent. of the 1,033 cases had tubercle bacilli in the sputum. He also examined 15 cases of thoracic contusion and found among them 9 cases of tuberculosis, in all of which a causal relationship between the trauma and the localization of the tuberculous process could be established. Among the 1,033 Leysin cases there were 3 examples of thoracic contusion, all of which showed definite evidence of pulmonary tuberculosis. The most difficult question to settle was the lapse of time which intervened between the traumatism and the first symptoms of pulmonary tuberculosis. This interval undoubtedly varied considerably in different cases, and it appeared impossible to determine a maximum period applicable to all cases.

According to Fein, who showed a case in a youth of 18 at the Vienna Laryngo-Rhinological Society, isolated **tuberculosis of the tonsil** is a rare event. Such cases are frequently quoted in support of the view that the tonsils are the portal of entry for tuberculosis. On close examination, however, it will usually be found that in addition to the tonsillar focus which is regarded as primary there is also a focus in the lungs, so that the hypothesis of a tonsillar origin falls to the ground. Even in Fein's case there was an extinct tuberculous focus in the right apex. It is, therefore, impossible in such cases to determine whether the primary infection was in the tonsil or the lung, or whether both organs were infected from another unknown portal of entry. Examples of apparently isolated tuberculosis of the tonsils should be regarded with reserve, as the presence of latent foci in the lungs can never be excluded.

Austin examined the excised tonsils of 45 children aged from 2½ to 15 years, who were clinically non-tuberculous, for the presence of tuberculosis by inoculation of guinea-pigs, histological examination of sections, cultures on Dorset egg medium and direct smears. In none of the cases did histological examination show any evidence of tubercle and no tubercle bacilli were found in any of the cultures or direct smears. The inoculation was positive in only one case, the organism being the human type of the tubercle bacillus. Although tuberculosis of the tonsils in children is not rare, in most of the cases tuberculous lesions are found elsewhere in the body, especially in the cervical lymph glands. The occurrence of the tubercle bacillus in the tonsils of children without clinical evidence of tuberculosis is not frequent. The discovery by Mitchell of tubercle bacilli in the tonsils of 13 out of 100 children without signs of tuberculosis is attributed by Austin to the fact that tubercle bacilli were prevalent in the Edinburgh milk supply, whereas the children in Austin's series came from a community where the supply of cow's milk was less likely to be contaminated. Moreover, only two of the cases came from families in which there were other cases of tuberculosis, and none of the children gave clinical evidence of tuberculosis.

Morbid anatomy. Canti carried out 84 autopsies on children up to 10 years of age, an abnormally large proportion, 33 cases, or 39·30 per cent. being under 1 year. 16 or 19·05 per cent., showed tuberculous lesions. In 10 cases the foci were in the lungs, and in 6 there were no lung foci exclusive of miliary tuberculosis. 7 of the 10 cases showed no tuberculous lesions outside the thorax, and 3 showed lesions in or in connexion with the alimentary tract. The findings in Canti's series agreed substantially with those of Ghon, and constituted strong evidence in favour of the common existence of primary pulmonary tuberculosis in children, the outstanding feature being as follows: (1) The almost constant finding of a lung focus when tuberculous mediastinal glands were present and the close relation of these glands to the lung focus. (2) The frequent singleness of the lung focus. (3) The constant finding of tuberculous mediastinal glands when a lung focus was present. (4) The almost constant absence of a lung focus when the portal of entry appeared to be elsewhere. (5) The almost constant absence of evidence that the portal of entry might be elsewhere when a lung focus was present.

Hart records the results of 573 autopsies personally conducted with a special view to tuberculosis on the mixed material of a field hospital. This figure excludes a few cases of known pulmonary tuberculosis. Every care was taken to locate the least tuberculous lesion, and out of the 573 autopsies 196, or 34 per cent., showed recent or obsolete tuberculosis. Of these, 80 per cent. were obsolete lesions of the lung or thoracic glands.

Now these young men of military age came from all over Germany and largely from the country districts, but 34 per cent. is obviously a very different figure from the 60–70 per cent. quoted by the more moderate observers on hospital material in large towns. It agrees well with Rössle's 33 per cent. for military autopsies, and while realizing the special nature of his material, the author cannot see his way (*pace* Naegeli) to concede even a town rate of more than 50 per cent. for the whole population. What then of the tuberculin test figures? They must result from *bacillary* *invasion*, as opposed to infection (Orth), that is to say, capacity for reaction to tuberculin must come from the mere presence of bacilli in the body, not necessarily accompanied by localized lesions excited thereby.

An interesting finding was the occurrence among these young men of 27 cases of spreading caseous lymph-gland tuberculosis. In 13 of these tuberculous meningitis was found, and in 5, acute miliary disease. The clinical picture in fact was characteristic of a much earlier age-period. But careful search showed always a primary lung focus, and the author regards these cases as an adult replica of primary aerogenous infection in children. He believes primary tuberculous infection to be parallel in the young and in the adult, and he adheres to his opinion that the peculiarity of adult apical phthisis consists in the fact that it is the result of an aerogenous reinfection in an organism already immunized. He regards as unproven the theory that endogenous reinfection is the usual mode of production of apical phthisis.

Symptomatology. Scott discusses the **diurnal variations in body weight** in tuberculous patients in a paper based on his observations at a tuberculosis dispensary. The patients were weighed between 2 and 4 in the afternoon, and again between 10 and 12 next morning. Out of a total of 962 recorded weights, 146 showed no variation, 205 showed an increase, and 611 a decrease. The average increase was 0·77 lb. and the average decrease 1·03 lb. The cause of the variation was obscure. The decrease was greatest from the age of 20–24, and was proportional to the severity of the infection.

The influence of high air temperature on tuberculosis. Gauss investigated the temperature of 56 tuberculous patients in the Cook County Hospital, Chicago, during the heat wave in July 1916. In the five days preceding the heat wave, viz., July 20–25, the average afternoon temperatures varied between 99·5 and 100; in the five days of the heat wave, viz., July 26–30 the afternoon temperature was between 100·5 and 100·9, and in the five days after the heat wave between 99·7 and 100. During the heat wave the average afternoon temperature was 100·62 as compared with 99·8 and 99·86 for similar periods preceding and following it. Gauss concludes that the increased temperatures for July 26–30 were probably caused by the high air temperature and unfavourable atmospheric conditions.

Hypertension in tuberculosis. Although a low blood-pressure is the rule in pulmonary tuberculosis, a small group of cases present a remarkable hypertension. Colbert, in a series of cases of tuberculosis, found 15 cases or 5 per cent. with a rise of blood-pressure exceeding 18 with Pachon's oscillometer. In some the maximum blood-pressure was as high as 25 or 26. The minimum as a rule was slightly increased, but hardly ever exceeded 11. The difference between the maximum and minimum blood-pressures might, therefore, be considerable. The hypertension was not dependent on any other cause, such as obesity, atheroma or renal disease, but was attributed by Colbert to disturbance of the function of the organs regulating blood-pressure by a specific microbial secretion. A constant symptom in these cases of hypertension was a tendency to haemoptysis of varying degree. The prognosis of this form of tuberculosis is favourable. Contrary to what is seen in cases with hypotension, an appreciable fall of the maximum tension regularly takes place, the minimum tension falling much less as the patient improves. This fall of blood-pressure is a favourable sign, unless the tuberculosis is associated with a hypertensive disease such as diabetes.

Under the term 'periphrenitis' Loeper describes a localized form of **tuberculous peritonitis** which often simulates hepatic or renal disease, or more frequently still, affections of the stomach and colon. The term periphrenitis is derived from the localization of the tuberculous process on the two surfaces of the diaphragm, in the cellular tissue surrounding the diaphragm, and sometimes even in the diaphragm itself. In its gastric form it may simulate gastritis, gastric ulcer, and in its intestinal form mucomembranous enteritis or the obstinate forms of flatulence and meteorism described by Denéchau (vide *Medical Supplement*, 1919, **2**, 177 *b*). The diagnosis in such cases is made not by exclusive examination of the alimentary canal but by a study of the chest and general condition, including X-ray examination of the lungs and pleura.

The prognostic importance of **tuberculosis of the larynx** is emphasized by Sir St. Clair Thomson who recommends that every tuberculosis sanatorium should have a laryngologist on its regular staff. The after-history of 833 consumptive patients examined by him at Midhurst Sanatorium between 1911 and 1915 showed that the mortality in cases with laryngeal involvement which occurred in 22·2 per cent. of all admissions to the sanatorium was 42·9 per cent. in Group I of the Turban-Gerhardt classification as compared with 15·6 per cent. in the non-laryngeal cases. In Group II the mortality rose from 38 per cent. for the non-laryngeal cases to 63·3 per cent. for the laryngeal cases, and in Group III from 70·4 to 78·3 per cent. Taking all three groups together, the presence of tuberculosis in the larynx raised the percentage of deaths during the 3 to 7 year period after discharge from the sanatorium from 39·7 per cent. to 68·9 per cent.

Mahelin, assistant in the Service of Laryngology of the American Commission for the Prevention of Tuberculosis in France, has devoted her Paris thesis to the study of the mild and curable forms of tuberculous laryngitis, which include early cases, chronic forms, and those which show no tendency to progress. She points out that the diagnosis in these cases is of considerable difficulty owing to the complete absence of any functional symptoms, the presence of superadded lesions, the difficulty of biopsy, and the uncertainty of the results of histological examination. She therefore recommends that a search should be made for these mild and curable forms of tuberculous laryngitis by making a systematic examination of the larynx in all cases of tuberculosis.

Recoveries from **tuberculous meningitis** are occasionally recorded. Martin, in 1909, collected 20 cases in which the diagnosis was confirmed by the presence of tubercle bacilli in the spinal fluid, by inoculation of guinea-pigs, by later post-mortem findings, or by the ophthalmoscope. Browning gave the number of undoubted recoveries reported up to 1914 as 80. They included, however, 14 of his own in which the diagnosis cannot be accepted as confirmed. Van der Bogert, from whose paper the above information has been taken, reports a case in a girl aged 3½ years in whom the symptoms indicating tuberculous meningitis were marked irritability and sensitiveness to external irritation, distinct neck rigidity and irregular remittent temperature. The cerebrospinal fluid showed lymphocytosis, and two typical tubercle bacilli, and inoculation of a guinea-pig proved positive. Rapid improvement took place after a second lumbar puncture, and a slow but uninterrupted recovery took place. When seen six months after the onset the child was well, though mentally excitable.

Lesage, who apparently upholds the classical doctrine that tuberculous meningitis is invariably fatal, maintains that before speaking of a recovery from this condition, one must be absolutely certain that there is not an error in diagnosis as there are many curable conditions which may simulate tuberculous meningitis. He considers that no case should be accepted as a recovery unless it is stated that a positive inoculation was obtained with a *healthy* guinea-pig. In many laboratories he has found that guinea-pigs have been bought as new, although they have already been inoculated with tuberculosis. Moreover, some of the cases of so-called recoveries should probably be regarded as remissions, Morquio having reported a case in which the remission lasted 18 months. The presence of an area of sclerosis found when death takes place several years after a meningeal attack is not necessarily a proof of its tuberculous nature, as non-tuberculous meningeal processes may also be followed by sclerosis. Lastly, Lesage suggests that the organism found in some of the cases was an acid-fast non-tuberculous bacillus.

In his Paris thesis Vincentelli records several cases to show that involvement of the meninges frequently occurs in the cachectic stage of chronic tuberculosis in the adult when the tubercle bacillus attacks several viscera simultaneously. Symptoms of meningeal involvement during life and post-mortem evidence of tuberculous infection of the meninges may be absent, but inoculation of guinea-pigs with the cerebrospinal fluid yields a positive result. On the other hand, a series of meningeal phenomena, such as headache, backache, torpor, Kernig's sign, vomiting and constipation may occur in the course of chronic pulmonary tuberculosis in the adult, and yet recovery takes place. Sometimes, however, these phenomena are merely the prelude to an attack of tuberculous meningitis which follows the ordinary course.

Cases of tuberculous meningitis in which polymorphonuclear leucocytes predominate in the cerebrospinal fluid are not very common. Massias, who has collected a number of examples from French and Italian literature, records a case in a woman aged 33 which was characterized by its rapid course simulating cerebrospinal meningitis and the almost exclusive presence of polymorphonuclears and great abundance of tubercle bacilli in the cerebrospinal fluid. Death took place after four days' illness. In addition to meningitis the necropsy showed fibro-caseous lesions of the left apex and caseous hilar glands. There was no thoracic or abdominal miliary tuberculosis.

Loygue reports a case of tuberculous meningo-encephalitis in which the disease was mistaken for lethargic encephalitis during life owing to drowsiness, ptosis and convergence, while the intrinsic ocular muscles remained intact. The limpidity of the cerebrospinal fluid, its relatively scarce albumin content and absence of cellular reaction were against the diagnosis of cerebrospinal meningitis and tuberculous meningitis, while syphilis was excluded by a negative Wassermann reaction in the blood and spinal fluid. At the necropsy no tubercles were seen in the brain with the naked eye, and it was only on microscopical examination that tuberculous meningo-encephalitis and tubercle bacilli were discovered.

Rominger of the Freiburg University Paediatric Clinic attaches special diagnostic value to Pándy's reaction which is carried out as follows: a drop of the cerebrospinal fluid is added to 1 c.c. of a concentrated solution of carbolic acid (1 part of carbolic acid crystals plus 15 parts of distilled water).

If the reaction is positive, a bluish-white cloud forms in a few seconds at the point of junction of the two fluids, showing that globulins are present in abnormal amount. In all the 15 cases of tuberculous meningitis observed at the Freiburg Clinic within the last 9 months Pándy's reaction was positive. On the other hand, in 53 cases in which it was negative, the case proved not to be tuberculous meningitis. The reaction is not specific, as it may be found in any cerebral or meningeal affection with a pathological increase of albumin in the cerebrospinal fluid. Its value, however, lies in the fact that a positive result may be obtained before any pathognomonic signs of tuberculous meningitis, such as the presence of tubercle bacilli in the spinal fluid or the typical X-ray appearances in the lungs, while a negative reaction excludes tuberculous meningitis.

The muscular system in tuberculosis. According to Verrienti muscular hyperexcitability is a phenomenon which is present in all stages of the infection. It may be seen in all the muscles of the body, but is most pronounced in the thoracic muscles, especially the supraspinatus, pectoralis major and trapezius. Involvement of the cardiac muscle is shown by the readiness with which it responds to stimuli, the pulse being always abnormally frequent. The hyperexcitability of the smooth muscle fibres is illustrated by the flushing of the cheeks, turgescence of the veins, and frequent evacuations caused by increased peristalsis apart from any localization of the tuberculous process. Owing to the frequency of muscular hyperexcitability at an early stage, Verrienti does not hesitate to regard it as an important sign in the early diagnosis of the disease.

Halbron, Pradal, and Théodorescu are inclined to attribute considerable diagnostic and prognostic importance to the myotonic reaction (Loeper and Codet) or myo-oedema (F. Lévy) seen in pulmonary tuberculosis in the trapezius, biceps and adductors of the thigh. Sainton, on the other hand, points out that though myo-oedema is frequent in phthisis, it is met with in numerous other morbid conditions, such as alcoholism, cancer, various infections, nephritis with uraemia, lethargic encephalitis, severe acute articular rheumatism and certain forms of chronic rheumatism, and Addison's disease. The three conditions in which it is most persistent and intense are typhoid fever, chronic pulmonary tuberculosis, and plumbism. Sainton attributes the phenomenon to neuromuscular hyperexcitability caused by an intoxication of endogenous or exogenous origin, but emphasizes the fact that it is a symptom of any intoxication, and that in tuberculosis other factors such as concomitant infections or intoxications may supervene and modify its significance.

Tuberculosis and influenza. Fishberg sums up in a very clear paper the universal experience of the effect of the pandemic of 1918–19 on pulmonary tuberculosis, and adds some interesting clinical details from his own practice. He concludes in opposition to the older teaching that epidemic influenza has no aetiological relation to tuberculosis, and is not to be considered as a reactivator of dormant tuberculous lesions. Liability to contract influenza was certainly not found to be greater in tuberculous patients than in others, and the prognosis with regard to the epidemic seemed better in tuberculosis and other chronic respiratory diseases than among the normal population.

With regard to the activation of tuberculous lesions, the frequent dating of phthisis from an attack of influenza was found to be deceptive. The supposed attack was not found on careful inquiry to correspond with the type of influenza prevalent in Europe and America during the last two years; namely an affection primarily of the upper respiratory tract with a later and less frequent descent to the bronchi and lungs. In all cases the pseudo-influenza described by the patients was typical of tuberculosis itself, and Fishberg states that he has seen no single case where phthisis could be ascribed to a previous influenzal attack.

Many cases with post-influenzal pulmonary lesions have been confused with tuberculosis. But in these the signs are predominantly in the lower lobes, and the extent of the lesions is suspiciously large compared with the constitutional symptoms present. Post-influenzal lesions as a whole were found to cause less change to percussion than to auscultation. Even when situated in the upper lobes, resonance above the clavicle remained unimpaired. They were mostly catarrhal or bronchiectatic in character, with rare localized empyemata and rarer lung abscesses.

Tuberculous patients passed through influenza in a surprising way. The author saw several recover with pneumonia and ‘heliotrope cyanosis’, and cases with an artificial pneumothorax were not seriously embarrassed. Even a tuberculous woman six months pregnant survived influenzal bronchopneumonia, and gave birth to a healthy child.

Kayser-Petersen of Frankfort, who has seen 11 cases of influenza developing in cases of pulmonary tuberculosis, agrees with most writers that the course of influenza depends mainly on the character of the tuberculous process. Incipient disease of the apex and mild forms of fibrosis are usually not affected, whereas severe cases of pulmonary tuberculosis usually take a turn for the worse. In the writer's cases of activation of latent tuberculosis after influenza physical examination and especially the X-rays showed a central localization of the disease. Kayser-Petersen attributes this to the fact that influenza like measles is accompanied by a considerable swelling of the mediastinal lymph glands which may form a *locus minoris resistentiae* for the invasion and dissemination of tuberculosis.

As regards the effect of influenza on cases of artificial pneumothorax Burnand (1) director of the Leysin Sanatorium states that out of 20 patients with artificial pneumothorax who contracted influenza in November 1918, 6 died, death being due to development of pneumonia in the healthy lung. The other 14 cases recovered, although most of them developed complications of varying degrees of severity in the previously unaffected lung. These figures show that subjects of pneumothorax are not so susceptible as was once thought to intercurrent disease and that the supervention of an acute process in the healthy lung does not necessarily involve a fatal issue.

The relation of lupus erythematosus to tuberculosis. Fönss, who gives a long digest of the literature of his subject, has investigated several cases of lupus erythematosus and vulgaris at the Finsen Institute in Copenhagen with special reference to tuberculin tests. His digest of the literature shows that tubercle bacilli have never been found in the eruption; no irrefutable proof has been adduced that the various acid-fast bacilli described by certain observers were none but tubercle bacilli. Only in seven cases (Gougerot 2, Ehrmann and Reines 1, Bloch and Fuchs 4) has inoculation of guinea-pigs with an extract from the eruption led to the development of tuberculosis. The number of negative results is probably legion, for of late the relationship of the two diseases has been investigated with great industry. No one has ever found the characteristic microscopical manifestations of tuberculosis in the eruption. In the overwhelming majority of cases, subcutaneous injections of tuberculin have failed to provoke a focal reaction in the eruption. Fönss has investigated 12 cases of lupus erythematosus, injecting subcutaneously as much as 20 mgm. of tuberculin, but only in two cases did he see a focal reaction, and neither was absolutely characteristic of the focal reaction of tuberculosis to tuberculin. He notes, however, that the focal reaction is too uncertain, even in such a definitely tuberculous condition as lupus vulgaris to be a very reliable test; out of 69 cases of lupus vulgaris tested with tuberculin, he got a typical focal reaction only in 56. In nine cases it was atypical, and in four it was absent. A phenomenon suggesting a causal relationship between lupus erythematosus and tuberculosis is the dissemination of the eruption after an injection of tuberculin, as observed by McKee, Hoffmann and Bruusgaard. Fönss records the case of a man of 63, who had suffered in childhood from cervical adenitis with suppuration. In the scar which resulted, lupus erythematosus developed many years later. The coincidence of lupus erythematosus and definite signs of tuberculosis in the same person is variously estimated; some writers have found evidence of tuberculosis or of a prolonged exposure to infection with tuberculosis in 18 per cent. of their cases of lupus erythematosus. Others put this ratio as high as 17 per cent. His own observations and his study of the literature have led Fönss to conclude that in a few cases of lupus erythematosus the eruption has in all probability been provoked by the tubercle bacillus. But in most cases there is no positive evidence of tuberculosis as an exciting cause, and the negative evidence, as shown by the rarity of focal reactions to tuberculin, is definitely against the hypothesis that lupus erythematosus is a manifestation of tuberculosis.

Tuberculosis in women. According to Pommier the effects of pulmonary tuberculosis on the various periods of a woman's life may be summarized as follows: 1. Puberty. (*a*) In girls who are tuberculous or predisposed to tuberculosis there is usually a delay in the appearance of menstruation. (*b*) Chlorosis, mitral stenosis and scoliosis are frequently present at the same time. (*c*) On or before the appearance of the first menstrual period there may be pulmonary congestion, rise of temperature and haemoptysis. (*d*) Pulmonary tuberculosis at this period is apt to assume a particularly rapid and severe course. 2. Menstruation. (*a*) In the tuberculous subject there is a tendency to irregularity, diminution or disappearance of the menstrual periods. (*b*) In some cases the temperature rises at this time. Various types of pyrexia are met with, but as a rule the rise of temperature precedes the appearance of menstruation, and is given the name of premenstrual fever. (*c*) This fever is accompanied by a recrudescence of the pulmonary symptoms and sometimes by periodic haemoptysis. (*d*) This aggravation of the disease may disappear with the menstrual period, persist indefinitely or constitute the onset of a severe form of the disease. 3. Pregnancy. (*a*) The prognosis of pregnancy varies with the degree of tuberculosis. In severe forms there is a liability to abortion and premature confinement. (*b*) The infant is not born tuberculous, but is often very weakly and its mortality is high in the first year of life. (*c*) Pregnancy exercises an unfavourable influence on pulmonary tuberculosis, aggravation of the disease being most likely to occur in the second half of pregnancy owing to decalcification, glycaemia and diminution of tuberculous antibodies. The prognosis is also unfavourable in young women, in pregnancies at short intervals, and in cases with laryngeal involvement. 4. Parturition.

(*a*) Labour is retarded by the exhausted condition of the patient, or in some cases is accelerated as the result of uterine atony and there is a tendency to post-partum haemorrhage. (*b*) Delivery may give rise to serious complications such as fulminating haemoptysis, asphyxia, sudden death from pleuro-pulmonary adhesions and pneumothorax. 5. Puerperium. (*a*) Tuberculosis creates a state of diminished resistance which is favourable to puerperal infection. (*b*) Frequently it assumes a very rapid course in the form of caseous pneumonia or acute miliary tuberculosis. 6. Lactation. (*a*) The milk secretion is generally normal, and with a few exceptions the milk does not contain tubercle bacilli. 7. Menopause. (*a*) The menopause is early in tuberculous women. (*b*) Pulmonary tuberculosis occurring at this period is usually the reactivation of a disease which first appeared at puberty.

Begtrup-Hansen sums up a long experience of the phenomena connected with pregnancy in tuberculous women. The paper includes a tabular presentation of nearly 300 cases, with a historical introduction and survey of the literature.

Pregnancy is found to have some effect on all but the least active cases of phthisis, but this effect differs considerably at the different periods involved. The two specially dangerous times are the first third of pregnancy and the puerperium, while the latter part of pregnancy is often marked by considerable clinical improvement. The author establishes a parallel between these favourable and unfavourable times and the post- and pre-menstrual periods. In the first third of pregnancy and the puerperium, the pre-menstrual type of temperature prevails, with a metabolic tendency towards protein loss. The periods are alike in being unfavourable. On the other hand, during the latter part of pregnancy the temperature is of post-menstrual type, the metabolic tendency is toward protein storage, and the general indications are favourable.

It is of course most important for a pregnant woman with active phthisis to be under sanatorium care, and far too often this is not the case. If proper care in a sanatorium is available, the indications for interrupting pregnancy are few and limited to special cases.

Nobécourt and Paraf carried out the cuti-reaction on 100 women in the fifth to ninth month of pregnancy with the following results: (1) In 32 cases the reaction was negative. 22 of these were women from the country who were obviously free from tuberculosis, and the remaining 10 were suffering from a severe form of tuberculosis which subsequently proved fatal. (2) In 68 the reaction was positive. Pregnancy therefore has a distinct influence on the cuti-reaction in the course of ulcero-caseous tuberculosis, as patients with this form of the disease showed only negative reactions, whereas as a rule the reaction in such cases is positive or at least faint (cachectic reaction). In 15 per cent. the cuti-reaction was affected by delivery. In women with ulcero-caseous tuberculosis the cuti-reaction, which was negative before delivery, remained so afterwards. Moreover in 11 women who showed no clinical evidence of tuberculosis the cuti-reaction became negative or less marked after delivery, and in 3 the diminution of the reaction coincided with the appearance of a tuberculous manifestation, such as pleurisy or pleuro-pulmonary congestion. In some cases therefore pregnancy and delivery give rise to a state of tuberculin anergy similar to that caused by some infectious diseases, especially measles (von Pirquet), or influenza (Debré). The investigations of several writers such as von Pirquet, Rolly, Roepke and Wolff-Eisner, and Léon Bernard have shown that the diminution in sensitiveness to tuberculin is usually associated with a diminution of immunity. This state of anergy which is particularly marked after delivery may explain the aggravation which the tuberculous process undergoes at this period.

In an article on **conjugal tuberculosis** Ward, tuberculosis officer for South Devon, maintains that it is direct infection and not predisposition which is the most important factor in the spread of tuberculosis, and that infection is correspondingly more frequent in a case of man and wife where the exposure to it is greater and more prolonged. Of 156 cases in which the mate of a tuberculous husband or wife was examined, 91 or 58 per cent. were found to be tuberculous, 16 or 10 per cent. suspect, and 49 or 32 per cent. negative. Ward holds that the great majority of the mates of tuberculous husbands or wives sooner or later show signs or develop symptoms of tuberculosis, but believes that the great majority of those infected, recover, and make a speedier recovery than most tuberculous patients probably owing to the enhanced immunity conferred by graduated doses of bacilli.

Diagnosis. Vargas, professor at the General Pathologic Clinic of the National University of Columbia, describes a new diagnostic sign in incipient cases, which consists in the reinforcement of the whispered voice in the affected lung. The sign, which must not be confused with whispered pectoriloquy, appears at the beginning of the tuberculous process in the lung when the X-rays do not even give a distinct shadow and when there is not any other sign obtained by percussion or auscultation.

In a centre for examining tuberculosis cases Roubier submitted 120 men to a marching test and found the following five varieties of reaction: (1) Moderate transient reaction. The temperature rises seven or eight tenths of a degree Centigrade after one hour's march, but becomes normal after an hour's rest (normal reaction or negative test). (2). Transient exaggerated reaction. The temperature rises more than seven or eight tenths of a degree, exceeds 100·4 and sometimes rises to 102·2, but returns to normal within an hour. This type of reaction is observed in nervous subjects and has not much significance. (3) Persistent reaction. The temperature after the march does not subside after an hour's rest, and remains more than four or five tenths of a degree above the initial temperature (positive reaction). (4) The temperature, which has risen after marching, continues to rise when the subject is at rest (paradoxical reaction). (5) The temperature after marching remains the same as before. The last two types are both very rare. Roubier came to the conclusion that when the tuberculous lesions were active the test was positive, and that it was negative when the lesions were extinct or fibrosed. The test, however, was positive apart from tuberculosis in cases of debility, asthenia, convalescence, and especially in tachycardia and incomplete Graves's disease. Although the test was not pathognomonic of tuberculosis, it was of value in giving information as to the ability of the organism to support fatigue.

Boez and Duhot performed the reaction of complement fixation on 141 cases of suspected or definite tuberculosis and on 60 persons who were healthy or had other affections than tuberculosis, with the following results. The reaction was positive in 77·90 per cent. of the cases of definite tuberculosis. In the first stage of the disease it was positive in 77·77 per cent., in the second in 82·05 per cent., and in the third in 63·6 per cent. Apart from syphilitic cases in which the reaction was relatively frequent, especially if the Wassermann reaction was positive, patients with non-syphilitic affections furnished only 7·69 per cent. of the positive results. The frequency of the reaction in tuberculosis as compared with its rarity in non-tuberculous affections shows that the reaction is of considerable diagnostic value though not absolutely reliable.

Salomon has tested the albumino-reaction for tuberculosis in 418 cases concurrently with other diagnostic methods, and came to the following conclusions: Patients whose sputum persistently gave a negative reaction could not be regarded as carriers of tubercle bacilli. A positive reaction, however, might occur in a number of acute or chronic broncho-pulmonary affections, especially in acute inflammatory conditions of the lung, as well as in bronchitis and congestion of the lung in cardiac and renal disease. The reaction therefore does not supply any useful information as regards the diagnosis of acute pulmonary tuberculosis. In chronic pulmonary tuberculosis the reaction was constantly positive whatever the stage of the disease. Not infrequently it was readily obtained in cases in which tubercle bacilli were scanty, and only found after repeated examinations and homogenization. The reaction was very useful in the interpretation of apical pleurisy, and its results always tallied with the X-ray findings, whereas examination for tubercle bacilli in this group of cases was always negative. In fibrosis of the apices as shown by clinical signs and radioscopy, the reaction was not infrequently negative, even when it had been proved that the patients had had frequent attacks of tuberculosis. In those cases, however, a negative reaction indicated that the lesions were cicatrized. In chronic bronchitis, whether simple or associated with emphysema, fibrosis of the apices, or enlargement of the bronchial glands, the reaction was habitually negative. In such cases it served to exclude the suspicion of active tuberculosis. Salomon concludes that the albumino-reaction of the sputum should be used as frequently in tuberculosis departments as bacteriological examination of the sputum or radioscopy (vide also *Medical Science*, 1919, **1**, 165).

The method is carried out as follows: The sputum is collected in a dry vessel in as fresh a condition as possible. An equal amount of distilled or ordinary water is added, and the mass triturated with a glass rod. The mucus is coagulated by the addition of acetic acid, and the fluid filtered. To avoid errors, one or two drops of acid should be added to the filtrate. The albumin if present can then be coagulated by heat or potassium ferrocyanide or nitric acid.

Treatment. Kinghorn, of Saranac Lake, discusses sanatorium results and the use of rest and exercise in pulmonary tuberculosis, especially in the light of the results at the Brompton Sanatorium at Frimley. He is of opinion that the ordinary rest and walking exercise treatment in sanatoria gives better results than work therapy as practised at Frimley. He demands far longer periods of treatment, six, nine, or twelve months if possible, especially for those who are economically unable to resume work gradually. Sedentary occupations are possible for the majority of ex-patients, and show better results than those demanding much walking or heavy muscular work. Earlier diagnosis and more conscientious after-care are among the other points emphasized as essential to the improvement of sanatorium results.

During the last five or six years Burnand (2) has made a systematic use of **digitalis** at the Leysin Sanatorium in cases of pulmonary tuberculosis with a low blood-pressure. The drug is indicated in cases of low tension and tachycardia irrespective of the extent and character of the pulmonary lesions. Although the treatment has little or no effect in the terminal stages of tuberculous cachexia in which the cardiac fibre is irremediably degenerated, Burnand is convinced that phthisical patients treated by digitalis at a relatively early stage when the myocardium still possesses a certain vitality, derive considerable benefit from this treatment. Cases in which a systematic examination of the blood-pressure was made with Pachon's oscillometer showed a considerable rise of blood-pressure. The drug was administered in doses of 10 cgm. of the powdered leaves on 3 out of every 10 days, e.g. on the 1st, 2nd, and 3rd of each month, and then on the 11th, 12th, 13th, and 21st and 22nd and 23rd.

Stuhl has found that tuberculous effusions into the pleural or peritoneal cavities react favourably to **tuberculin,** the improvement being accompanied by increased diuresis. The ordinary small doses of Denys's or Rosenbach's tuberculin proved effectual, and it was dangerous to use the much stronger *Alt tuberkulin* usually employed for diagnostic purposes. The presence of fever was no contra-indication to the treatment.

R. C. Newton records 7 cases of tuberculosis in children aged from 6 years upwards, nearly all of whom showed very perceptible improvement with comparatively small or very small doses of tuberculin. Of 4 cases of peritoneal tuberculosis, 3 were brought under treatment within a few weeks of the appearance of the ascites and prompt improvement occurred, while the fourth case took longer to recover. Excellent results were obtained in the tuberculin treatment of 3 cases of pulmonary tuberculosis that came under treatment within a few months of the beginning of active pulmonary lesions, while cases of older standing although improving for a time under tuberculin failed to show a permanent arrest.

Perkins, Young, and Meek, treated 8 cases of pulmonary tuberculosis by **heteroserotherapy,** the fluid used being taken from other patients with tuberculous pleurisy. The injections were given subcutaneously in doses gradually increased from 1 c.c. to 10, 15, or even 25 c.c. At the commencement of a course of treatment they were given twice or thrice weekly; when larger doses were reached they were given as a rule at weekly intervals. No bad effects resulted. With one exception all the patients had extensive active disease of the lung, and the prognosis appeared very grave. In three cases no effect was produced, in two improvement coincided with treatment, but signs of improvement had appeared before it was commenced, and in three the favourable results could be fairly ascribed to the treatment.

In their monograph on **artificial pneumothorax** based on 113 cases on which the operation was performed at the Hauteville Sanatorium between July 1908 and March 1918, Dumarest and Murard state that out of 106 cases which could be followed up 50 were favourable and 56 unfavourable. Complete recovery occurred in 8 cases, or 7·55 per cent. In round numbers the method was able to save the lives of 50 per cent. of the patients and in about half of these the cure was permanent.

Henius, who has treated 24 cases of lung disease by artificial pneumothorax with remarkably good results, regards the following conditions as indications for the operation: (1) unilateral cavernous tuberculosis, even when there is slight disease in the opposite lung but with no tendency to extend. (2) Unilateral infiltrative febrile processes. (3) Unilateral caseous pneumonia (tuberculous pleuro-pneumonia). (4) Haemoptysis, when the side from which the haemorrhage comes can be determined. (5) Pleurisy with much effusion, air taking the place of the exudation. (6) Multiple unilateral bronchiectasis and central lung abscess.

Henius classifies the complications of artifical pneumothorax into those occurring (*a*) during, (*b*) after the operation.

(*a*) During the operation, (1) Gas embolism. This accident is very rare with the methods at present in use. Unilateral transient amaurosis often occurs, and the cases frequently end fatally. (2) Subcutaneous, deep, subpleural and mediastinal emphysema. This occurrence is not dangerous, with the exception of mediastinal emphysema which occasionally gives rise to circulatory disturbance. (3) Pleural eclampsia which is occasionally fatal.

(*b*) After the operation, (1) Pleural effusion. A small marginal effusion occurs in from 50 to 75 per cent. of all cases and is easily visible on the screen. As a rule the effusion, which is almost always serous, does not give rise to symptoms, but occasionally it may be so large that tapping is required. (2) Pulmonary haemorrhage, (*a*) through injury to the lung, when it is usually slight in amount, (*b*) from an insufficiently collapsed lung. (3) Occurrence of disease in the opposite lung. (4) Subsequent development of pneumothorax on the healthy side through a weak spot in the anterior mediastinum—a very rare occurrence. (5) Gastric disturbance through depression of the diaphragm. (6) Bilateral paralysis of the diaphragm. (7) Displacement of the heart. (8) Spontaneous pneumothorax on the same side as the artificial pneumothorax.

Thomas relates a case of cerebral gas embolism occurring during the performance of artificial pneumothorax. The symptoms developed at the eighth administration after 100 c. c. of gas had been introduced, and consisted of cyanosis of the face, slow and stertorous breathing, conjugate deviation of the eyes to the right, general rigidity and loss of consciousness. There was complete loss of sensation and reflexes. Consciousness returned on the following day and no untoward results occurred.

Parfitt and Crombie report on a series of cases of progressive pulmonary tuberculosis treated by artificial pneumothorax. 25 per cent. were classed as moderately advanced, and 75 per cent. as far advanced. Only 6 per cent. were clinically unilateral. The disease had been manifest for an average of slightly less than 3 years. Out of this rather depressing material it was hoped that the disease might be checked for a longer or shorter period in about half of the cases ; for the other half the treatment was purely palliative.

The authors protest against loading the statistics of artificial pneumothorax with purely operative failures. What we want to know primarily, is the value of a successful compression, to what extent it leads to durable results, and to what extent it affords symptomatic relief.

Among the satisfactory compressions in the present series, 43 per cent. are, at the date of publication, quiescent or better and 34 per cent. dead, as against 17 per cent. and 43 per cent. among the operative failures. Three-fourths of the patients who are able to earn their living entirely, or in part, belong to the group of successful compressions. The series includes of course some of the dramatic recoveries which encourage workers in pneumothorax, but the main point seems to be that in cases where pneumothorax proved to be practicable 60 per cent. or more showed an amelioration which could not otherwise have been expected in more than about 20 per cent.

The authors had about 20 per cent. of effusions, but the cases were not all checked by X-rays, the use of which they find desirable but not essential. They recommend replacement of fluid as soon as it becomes appreciable. Some cases of mediastinal emphysema, traumatic pneumothorax and other accidents are reported. Kuss's needle is recommended for primary fills, and special attention is drawn to the necessity of carefully watching the condition of the mediastinum.

The tenth Conference of Tuberculosis Specialists in Berlin, in connexion with the German Central Anti-tuberculosis Committee, occupied itself largely with surgical treatment of tuberculosis.

Leading a discussion on artificial pneumothorax, Harms of Mannheim made the following points with reference to technique and indications. He advocates direct puncture with the sharp needle and minimum force. Maximum first fill of 800 c. c. of air or nitrogen. oxygen not being considered necessary. Site of election the axillary line, 5th–6th interspace, or 2nd–3rd interspace according to the location of disease in the upper or lower lobe. Good X-ray control. Effusions to be tapped when they show no sign of absorbing. Careful avoidance of hypertension and care of the mediastinum.

There appears to be some relaxation in the demand for unilaterality of disease in considering the indications for treatment, but forms of tuberculosis with acute onset are better avoided. Tuberculous complications are a contra-indication, excepting laryngeal disease. Harms demands a minimum of 1½ years' treatment, and points out the necessity of ensuring that an adequate period of treatment is economically possible, especially in insured patients.

Mühsam of Berlin reported the results of nine **thoracoplastic operations.** The only technical point mentioned is that he removed periosteum in order to avoid callus formation in the neighbourhood of the resected rib portions. Of the nine cases four died soon after operation, five improved for as long as three years but later relapsed. Extra-pleural plugging was not found very successful. Extra-pleural plugging with plastic measures gives more promise of success.

Holmboe describes his experiences in the galvano-cauterization of pleural adhesions with the help of the thoracoscope of Jakobaeus. The path of the operator is not a smooth one. The adhesions, when located, may be too thick and fibrotic for the cautery, which tends to adhere in a manner very painful for the patient. The field of vision, at no time very extensive, may be completely blocked by smoke, and 'the patience of all concerned severely tried'. But while minor mishaps are many, the actual danger to the patient from more serious complications such as haemorrhage or pyopneumothorax does not appear to be large, assuming that care is exercised and adhesions cauterized as close to the parietal pleura as possible.

The author examined 27 cases with the thoracoscope, and decided to cauterize nine. Of these nine it appears that six or seven were operative successes (that is to say, that the division attempted was effected). and five were therapeutic successes, in that striking clinical improvement followed.

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ASCITES AND ITS SURGICAL TREATMENT

The general impression gained by reading what is said on ascites in medical text-books, and in articles by physicians, is a gloomy one. It is a complication which generally appears in a patient who is going to die. Paracentesis is a means of giving temporary relief to such a patient. Atrophic cirrhosis, due to alcoholism, may be expected to end the patient's life in a few weeks; such patients live to be tapped only twice or three times. Polyserositis has as bad an outlook, although life may be more prolonged. The attempt of surgeons to substitute a more active treatment than paracentesis is stated to entail an immediate mortality of 30 per cent. or more and to be generally a failure in those who survive the operation.

From a surgeon's point of view it is a pity that the term ascites with its old associations cannot be abolished, and that of chronic peritonitis with effusion substituted. There would then be suggested the necessity for an inquiry as to the cause of the chronic peritonitis. Instead of assuming a hopeless change in the liver, an exploration of the abdomen would be called for in order that the diagnosis might be completed.

Paracentesis affords little additional information, and repetitions of tapping should convince the most pronounced sceptic that he is not dealing with an acute disease. Whatever the precise variety, the patient is presenting to it a marked resistance. The completion of the diagnosis by abdominal exploration should be regarded as of immediate importance. By exploring the abdomen the surgeon has often lighted upon a cause which he could remove completely and so cure the patient.

No such mortality as 30 per cent. should be quoted as incidental to the procedure; it could only occur in cases submitted to operation too late, especially when splenectomy has to be done. The methods related below are no more severe than tapping and drainage. As for the cases regarded as hopeless, those with atrophic cirrhosis from alcohol, some are quoted below which have been benefited by surgical treatment.

Thus without endangering the lives of patients a venous anastomosis between the portal and general circulation can be established by which good results can be obtained; at least an increased interval between the tappings, or a long intermission, or the ascites may not return during a course of years.

Exploration as a means of completing the diagnosis has had advocates from the early days of abdominal surgery. In particular, in order to complete the diagnosis as to the cause of ascites, it was advocated by O'Callaghan in 1886, by Rutherford Morison in 1899, and by Monprofit in 1904.

Among the conditions which may be met with on exploration, and which in consequence of the discovery may be removed, are:

1. Gummata of the liver, less often of the spleen, or of the abdominal wall. Gummata may be found, although the Wassermann reaction has been reported negative; the naked eye observation may be confirmed by the microscopical examination of a piece removed; when the gumma has broken down, the semi-fluid portion may be removed. Then directed by the diagnosis antisyphilitic treatment may prevent a return of the ascites.

2. Tuberculous disease may be discovered, breaking down glands in the mesentery may be scraped away and the mesentery sutured, the spleen may be removed if affected; caseous material may be washed out from the peritoneum by irrigation; adhesions may be carefully broken down, or a lateral anastomosis made to promote a passage of the intestinal contents. Whilst more frequent in the young, the condition may be also met with in adults. The younger the patient, the more likely the prospect that the tuberculous affection may subside.

3. A hydatid cyst of the liver may have quietly ruptured into the peritoneal cavity; the peritoneal infection can be successfully treated before the parasitic cyst walls have become buried in dense adhesions and before there are complications by septic organisms.

4. Simple inflammation and ulceration of the intestines from the stomach down to the rectum may set up chronic peritonitis and effusion, without other marked sign. After being tapped several times a boy has been cured by removing an appendix which had previously exhibited no signs of being affected by chronic inflammation. Chronic ulceration of the duodenum, also of the sigmoid flexure, instead of perforating, has formed adhesions and been followed by chronic peritonitis and effusion. Separation of the adhesions and covering in of the raw surface has been followed by an arrest of the peritoneal effusion.

5. A case of ascites complicated by diabetes was found to be caused by chronic pancreatitis with the formation of pancreatic calculi.

6. In connexion with the ovary, besides the occurrence of ovarian cysts which may have been more or less definitely diagnosed before operating, there are cases which could not be recognized by any means short of surgical exploration. One woman after being tapped a number of times was shown to have papilliferous outgrowths from both ovaries, yet without any

enlargements to constitute tumours. The removal of the two ovaries cured the patient; the disease of the ovaries was not malignant. A woman was found to have a parovarian cyst which reached up to the xiphoid cartilage. There was one large thin-walled sac which covered and adhered to all the abdominal viscera, so that only a small portion of the wall could be removed for examination. After a prolonged period of drainage, the patient recovered, without fluid re-collecting in the cyst.

7. Chronic peritonitis with effusion is set up by several infective agents; it may follow puerperal or gonorrhoeal infection in women; pneumococcal peritonitis may persist after the primary pulmonary infection has subsided; cocci or some allied organism may set up the condition known as multiple serositis or polyserositis, the peritoneum being most markedly affected. In some cases the peritoneal membrane is found to have undergone little change; in cases of longer standing it is thickened, including a thickening of the capsule of the liver and spleen. In the former case, where the peritoneum has not greatly altered, washing out of the peritoneal cavity with removal of fibrin may suffice to cure. Long-standing cases, in which the peritoneum has become thickened, may be cured, when not too late, by establishing an anastomosis.

8. Early exploration is of marked service in cases of malignant disease. If done early enough, a gastro-intestinal malignant ulcer may be successfully excised. When the cancer is found to be irremovable, relief may be afforded and the progress of exhaustion consequent on the rapid peritoneal exudation checked.

9. It is often difficult to distinguish portal from biliary cirrhosis, and the latter may be discovered to be due to gall-stones. The gall-stones being removed the cirrhosis and tendency to ascites is arrested.

Eck's Fistula. The first to try by way of experiment to find a way of giving relief by surgery to cirrhosis and its complication ascites, was N. V. Eck (Ekk) of St. Petersburg. He united the portal vein to the vena cava: of his first eight dogs one survived. The special difficulty in the experiment is the clamping of the veins whilst an artificial varix is being made. One way of avoiding anything more than a momentary arrest of the venous flow is to insert a continuous suture in the form of a ring between the two veins. Immediately before tightening the two ends in order to knot and complete the ring of suture, the blades of fine-pointed embroidery scissors are passed, one into each vein within the ring formed by the suture. On closing the blades a cut is made uniting the lumen of the two veins. At the same moment the ends of the continuous suture are drawn taut, when the closed blades of the scissors can be withdrawn without blood escaping.

After Eck, experiments were made on the production of the fistula by Stonikow in 1882, Pavlov in 1892, when 20 dogs survived out of 50, Tansini in 1902, and Bernheim and Voegtlin in 1912. In addition to experiments from the physiological point of view, it has been attempted on patients. Hitherto the difficulties of carrying out such an operation have proved insuperable. Kocher declared the operation impracticable, Bier in 1911 abandoned the attempt on account of haemorrhage, Rosenstein in 1913 reported that he had made an Eck's fistula on a woman suffering from cirrhosis of the liver. But there was only temporary relief, apparently owing to secondary obliteration of anastomosis. Jeger in 1916, practising on the cadaver, found it easier to anastomose the inferior vena cava with the superior mesenteric vein, or to implant the superior mesenteric vein into the vena cava.

Talma's operation. In 1889 Talma, at Utrecht, suggested to van der Meulen the artificial production of adhesions by suturing the omentum to the abdominal wall. The operation caused death by shock in a few hours. Shelky in 1891 repeated the operation, but the man, being attacked by delirium tremens, tore open his wound and died on the 15th day after the operation. In 1892 Lens fixed the omentum in the abdominal wall, fluid reaccumulated and the patient was tapped several times before death, 5½ months after the operation. Talma himself in 1898 reported a case which had been operated upon for him by v. Eiselsberg. A boy aged 9 had atrophic cirrhosis, enlargement of the spleen, albuminuria and ascites, which rapidly reaccumulated. After five tappings a simple incision was made, but the fluid quickly re-collected. At a second operation the omentum and the gall-bladder were sutured to the abdominal wall. Numerous veins developed on the abdominal wall, and the ascites was not reproduced. As the spleen continued to enlarge it was fixed into the abdominal wall at a third operation, when it was noted that numerous vascular adhesions had formed between the omentum and gall-bladder and the abdominal wall. After this the spleen shrank. Two years later, the boy appeared in good health. There was no ascites, the abdominal wall presented large veins. The liver was still enlarged, but there was no jaundice or albuminuria.

Drummond and Morison operation. In 1894 Rutherford Morison operated on a late case under Drummond by scrubbing the surfaces of the liver and spleen and the opposing surfaces of the parietal peritoneum with a sponge. The patient lived for 19 months afterwards, during which paracentesis was done 69 times. There was no post-mortem examination. In 1895 a woman aged 39 with an alcoholic history had a hobnail liver, severe ascites and oedema of the legs. After several tappings, she was treated like the first case. She made a good recovery: after several more tappings the anastomotic circulation became established and she was exhibited at the Carlisle British Medical Association Meeting a year after the operation.

In 1899 Morison recorded a second successful case, also notes of a post-mortem examination. Later in the year he added two cases in which he had fixed the omentum, and although in both some fluid persisted, there was good ground for hope that a venous anastomosis would be established. In 1903 Morison described the case of a heavy drinker aged 52 who had had delirium tremens 2½ years before, since then he had abstained from alcohol. He had been in hospital for six months under medical treatment by purging, and by paracentesis 18 gallons 2½ pints had been removed at 14 tappings. The omentum was stitched to the abdominal wall and a hypogastric drain inserted. It was noted that the liver was firm but of normal size, the spleen enlarged to twice its size. He drained for six weeks, then fluid collected, and 4 months after the operation 10½ pints were drawn off. After that there was no further tapping. 3½ years after the operation, there had been no reaccumulation of fluid, the liver was adherent to the abdominal wall, the epigastrium presented veins dilated enough to show in a photograph. This dilatation was mainly on the right side, a truss on the left side serving to compress the epigastric veins.

Fixation of the omentum in the abdominal wall with temporary

drainage through the hypogastrium. A simple method, which does not lead to the early death of even a weak patient, consists in making an incision of not more than 2 inches in the epigastrium, and a puncture in the hypogastrium sufficient to admit the forefinger. Through these openings the abdominal cavity can be sufficiently explored, so that conditions previously referred to may be noted. If no indications for a larger incision are found, a small piece of the free margin of the omentum is drawn through the epigastric incision and is fixed in the subcutaneous tissue between the recti muscles by four absorbable sutures, the skin being united over it. A drain is inserted through the hypogastric opening. The following advantages are attached to the method, first and foremost the diagnosis that no condition exists which can be removed; a slight operation which does not accelerate the patient's death; the formation of ample anastomotic adhesions under favourable circumstances; temporary relief by drainage whilst the anastomosis is developing; freedom from intestinal obstruction. The artificial ventral hernia in the epigastrium does not enlarge; an incision of two inches limits the hernia and yet does not cause strangulation if only a little of the free margin of the omentum is drawn through. The omentum within the abdominal cavity does not form a band under which a coil of small intestines may become strangulated as might be the case if the opening were made below the umbilicus.

The following examples, all late cases under physicians at the Westminster Hospital, were operated upon as above. (1) Female, 19, under Murrell, had been treated for anaemia (R.B.C. 3,830,000) and leukaemia (W.C. 3,000), and mitral regurgitation. After a year ascites developed, when the abdomen was explored and then drained. The ascites quickly recurred, so a month later the omentum was fixed in the abdominal wall. Enlarged veins were noted a month after the operation. She regained good health and returned to her occupation. 16 months after the epiplopexy she relapsed with the enlarged spleen and cirrhosis of the liver of Banti, but without return of the ascites. This was confirmed at the post-mortem and the vascularized adhesions were well marked.

(2) Female, 48, diagnosed as syphilitic cirrhosis, had had ascites for four months and the fluid had rapidly accumulated after tapping. No further paracentesis was required for 6 months when 23 pints were drawn off. She died 9 months after the epiplopexy; the liver weighed 2 lb. 9 oz. and was densely cirrhotic, there was also perihepatitis and perisplenitis. There were extensive adhesions, but they were not very well vascularized.

(3) A most unfavourable case was that of a woman aged 30, suffering from alcoholic cirrhosis. At the operation the liver was found reduced to half its size. The patient was not made worse by the epiplopexy, no further fluid collected, she simply became weaker and died five weeks after the operation, when the condition of the liver was confirmed.

(4) Female aged 30, under de Havilland Hall. The 'ascites' began 4 years before, after child-birth, by chronic septic peritonitis with effusion. She was tapped four times, after which the omentum was fixed in the abdominal wall. As fluid re-collected after the removal of the drainage tube it was reintroduced for a little while. Then the anastomosis became established and there was no reaccumulation of fluid for two years. Meanwhile she presented a soft systolic murmur and slight oedema of the ankles. Then the ascites returned and she died, but there was no post-mortem examination.

(5) Male aged 35, under de Havilland Hall; ascites had followed on syphilis. Antisyphilitic treatment and tappings failing, epiplopexy was performed. Four years later the ascites returned, and after death there was found a general fibrosis of the peritoneum.

(6) Male, under Allchin. At the age of 24 he began to suffer from duodenal ulceration which healed, but 'ascites', i. e. chronic septic peritonitis, with effusion followed. A surgeon explored his kidney for haematuria; later his appendix was removed. After eight years epiplopexy was done, and when the veins on the abdominal wall had become enlarged he recovered good health. From being apparently a confirmed invalid he was able to resume his occupation and continued well.

(7) Female, 50, under de Havilland Hall. She had hypertrophic cirrhosis and ascites due to alcohol, for which she was tapped many times. After epiplopexy she continued to take alcohol as before, but the fluid did not reaccumulate. Four years afterwards she was readmitted with advanced and inoperable cancer of the breast from which she died, when the peritoneal cavity was proved to be free from fluid.

(8) Female, 32, under Purves Stewart, with alcoholic atrophic cirrhosis. At the epiplopexy operation the liver seemed about half the normal size. The patient left the hospital convalescent.

W. J. Mayo (1) (2) recorded 28 cases, in which the omentum was fixed in the rectus abdominis muscles. There were four deaths immediately following the operation, eight died soon afterwards. The remainder were benefited, and in five there was a good result.

Sapheno-peritoneal anastomosis. In 1907 Ruotte described the turning upwards of the proximal end of the saphena vein so as to form a direct communication between the lumen of the vein and the peritoneal cavity. To avoid regurgitation of blood, the valves near the end of the vein before its junction with the femoral vein must be competent. The effect of this operation is not clear. At a post-mortem examination on a case sometime after Ruotte's operation Mori found the end of the saphena vein in the peritoneal cavity absorbed and replaced by fibrous tissue. Schepelmann performed Ruotte's operation on a man of 65, suffering from arteriosclerosis and osteoarthritis. He had had already a slight attack of apoplexy; there was marked ascites and a trace of albuminuria. About half the fluid escaped at the operation, and there followed oedema of the abdominal wall and groin on the side of the operation. For about six weeks the ascites did not recur; then paracentesis had to be done several times before death, five months after the operation. At the post-mortem the implanted end of the vein was blocked by fibrin.

Simon has published the best results; of 25 cases half improved and some resumed their occupations.

Permanent Drainage through the Femoral Ring. In 1907 Essex Wynter for a case of alcoholic cirrhosis in a man aged 50, who had been unrelieved by medical treatment and paracentesis, proposed drainage through the femoral ring, which was carried out by Sampson Handley. There was some leakage from the wound and the man was tapped a week after the operation. Then the ascites was arrested, yet the thigh on the side of the operation was not rendered oedematous.

In a second similar case under Wynter, Murray inserted a decalcified bone tube into the femoral canal, and the patient was able to get about without further need of paracentesis.

Nash in 1913 adopted this method in two cases. A barmaid aged 48, besides taking alcohol, had had miscarriages and suffered from syphilis, Her abdomen began to swell in 1905; in 1909, after repeated paracentesis there was a spontaneous rupture at the umbilicus and a flow for 14 days. Meanwhile she was treated by iodide of potassium for gumma of the liver. In 1909 epiplopexy above the umbilicus was done, when besides the gumma of the liver, perihepatitis and perisplenitis was noted. After this operation paracentesis had to be repeated 14 times, 280 pints of fluid being removed. Then in 1910 a bone-bobbin was inserted into the femoral canal. In 1913 she was in good health, working as a housekeeper, and weighed 11½ stone. There had been no return of the ascites.

In the other case, of a barman aged 43, ascites developed in 1911 and paracentesis was repeated. In 1912 a bone-bobbin was inserted in the right femoral canal. After this he was tapped twice, 12 and 9 pints of fluid being removed. Then reaccumulation ceased, and in 1913 he was well with no return of the ascites.

Erasion and excision of an area of parietal peritoneum. If the procedure is restricted to scraping the parietal peritoneum, the anastomosis through adhesions may be insufficient. If a wide area is denuded of peritoneum there may be haemorrhage and shock, which in the patients under consideration may determine death. In 1899 H. D. Rolleston and G. R. Turner reported the case of a man aged 45 with a hobnail liver complicated by haematemesis and ascites, but neither the liver nor spleen was enlarged. After scrubbing the peritoneum the omentum was fixed between the liver and the diaphragm. Six months later the man was in better health, but still had a little ascites and oedema of the legs.

In the same year Neumann noted the case of a woman with atrophic cirrhosis, enlarged spleen and albuminuria complicated by ascites. The peritoneum was scraped, and the omentum sutured to the abdominal wall. Enlargement of veins became visible, and six months later there was no trace of ascites and the patient was in good health.

In 1902 Bush described the case of a man aged 53 with progressive cirrhosis, ascites, albuminuria, and oedema of the legs. He was treated in the same way as the patient under Rolleston and Turner. He died three years later of double pneumonia without return of the ascites. At the post-mortem the liver and great omentum were found firmly adherent to the abdominal wall. There were veins in the adhesions as large as a lead pencil forming a connexion between parietal and portal veins.

In 1913 Kumaris of Athens recommended the removal of a wide area of parietal peritoneum. One case died on the 22nd day after the operation from erysipelas of the face without any re-formation of fluid. Another case was well without ascites 6 months later. He added a successful case by Lorenz.

In 1916 Kalb of Stettin, in order to relieve cases of ascites resulting from malignant disease, selected the triangle of Petit, and from the abdominal aspect excised the parietal peritoneum and the muscular wall down to the subcutaneous tissue over an area corresponding to a crown-piece. This was done on both sides.

Case I.—A man of 26, suffering from advanced colloid carcinoma of the stomach, was tapped every eight days during three months and then every three days, 2–2·5 litres being removed each time. As a result of the operation an oedematous swelling formed in each loin the size of a fist, the urine increased from 200–300 c.cm. to 800–1,200 c.cm. No further tapping was required for between 3–4 weeks. When he died 6 weeks after the operation, there were 300 c.cm. of fluid in the peritoneal cavity.

Case II.—A man aged 50, also suffering from cancer of the stomach, during 8 weeks was tapped every week and 3–4 litres drawn off each time. After the operation no tapping was needed and the urine increased. At the post-mortem there were 600 c.cm. in the peritoneal cavity.

Case III.—A woman with carcinoma of the ovary was repeatedly tapped during half a year. No further tapping was needed before her death 7 weeks after the operation.

Drainage into the subcutaneous tissue of the abdominal wall. Stoney and Moorhead in Dublin adopted Sampson Handley's lymphangioplastic method for a man aged 20, suffering from the results of polyserositis, for which repeated tappings had become necessary. At the operation thickening of the capsule of the liver and of the peritoneum in general was noted. Several strands of silk were passed obliquely through the abdominal wall. Six weeks later 6½ pints of fluid were removed, after which the fluid did not reaccumulate and he was able to do farm work. Six months after the operation there was merely slight blueness of the lips, the liver was palpable but there was no reaccumulation of fluid nor oedema of the abdominal wall.

In 1910 Peter Paterson of Glasgow described the use of a perforated glass cylinder with a flange at each end which he had used for connecting the peritoneal cavity with the subcutaneous tissue. He had adopted it in preference to the alternative, namely, strands of silk. The lumen of the cylinders $\frac{1}{12}$ inch in diameter did not get blocked, and in cases both of cirrhosis of the liver and also of accumulation of fluid secondary to malignant disease the patients received relief.

The method may, however, induce a large fluid sac to form in the subcutaneous tissue.

Henschen described the case of a girl aged 15, in whom the peritoneal cavity was connected with the subcutaneous tissue by means of a glass tube. The skin over the outer end of the glass tube became oedematous and rugose. In the following three years the girl was tapped 20 times: she then presented a multilocular cystic swelling extending from the umbilicus downwards and overhanging the mons veneris, and the glass tube was loose in the sac. The distension was relieved by drainage. Five years after the operation, at the age of 20, she menstruated for the first time; she had grown up strong and presented no signs of heart or kidney disease. Tapping had been required at longer intervals of 3 or 4 months, and it was hoped that the ascites was in the course of disappearing. To avoid the cystic swelling, Henschen advised the insertion of the tube in the lumbar region. Schepelmann, after trying several other forms of tubes, adopted the aorta of a calf hardened in formalin which was inserted obliquely through the abdominal wall, one on each side of the umbilicus. He did not think the subcutaneous oedema of the abdomen wall which followed an objection to the method.

Ascites disappearing after splenectomy. W. J. Mayo (3) has described his experiences of splenectomy for splenic anaemia; many of the cases were complicated by cirrhosis of the liver and in five cases ascites completely disappeared after splenectomy. The spleen usually contributes $\frac{1}{4}$–$\frac{1}{6}$ of the blood entering the liver by the portal vein. But when enlarged the blood from the spleen may come to equal that contributed by the superior mesenteric vein. Hence splenectomy may relieve an overloaded liver and so arrest the progress of cirrhosis and ascites if the cirrhosis has not already advanced too far.

Of 61 cases in which splenectomy was performed 7 (11·7 per cent.) were fatal, owing to extensive thrombosis of the superior mesenteric, splenic and portal veins, the cases in fact being too late.

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W. G. S.

SURGERY OF THE BREAST

Recent communications on the surgery of the breast deal with the confusing and useless character of the present terminology, the need for a more thorough histological examination, the results of the newer methods of operating for cancer, and the treatment by radiology. The connective tissue tumours which sometimes arise in the connective tissue of the breast, fibroma, lipoma, endothelioma, do not belong to the mammary gland as such.

1. **The terminology applied to swellings of the breast, both naked eye and microscopic.**

The normal histological characters of the breast vary with the period of life (1) the foetal breast; (2) the resting stage; (3) the stage of menstruation; (4) the lactation stage; (5) senile atrophy.

The stage of menstruation has been supposed to be the result of a stimulus by an ovarian hormone, similarly that of the stage of lactation by a stimulus derived from the pregnant uterus.

During lactation the ducts may become blocked by curd causing retention; micro-organisms find their way up the ducts, suppuration follows.

Senile atrophy is complicated by cystic formations owing to irregular constriction of the ducts by fibrous tissue.

Except for the above simple and obvious causes nothing can be said to be known concerning the origin of chronic inflammation and new growths of the breast.

It is this absence of knowledge as to the essential causes that renders the present terminology so unsatisfactory. MacCarty with others of the Mayo Clinic have noted down something like 100 different terms which have been applied to chronic inflammatory swellings and so-called benign tumours of the breast. The names applied to cancer of the breast are only less numerous and are equally useless and misleading. The distinctions drawn really provide no advantage, either as regards treatment or prognosis. Moreover nothing is gained by the distinctions attempted to be drawn from microscopic examinations. Bloodgood said that he submitted 69 specimens on the border-line between benign and malignant growths to a number of pathological colleagues and in no single case was there uniform agreement as to whether the lesion was benign or malignant.

In the absence of knowledge as to causation there are three divisions determined by the method of surgical treatment, and these correspond with three distinctions which it is necessary to make both in clinical and microscopic examinations.

(1) Inflammation of the breast in which some treatment short of removing the breast is indicated. The essential appearances under the microscope lie outside the basement membrane of the alveoli. The basement membrane shuts off the epithelial gland elements which are not primarily affected.

(2) Benign tumour formation in which the treatment is that of excision of the breast. It is characterized by changes in the epithelium of the alveoli and ducts within the basement membrane.

(3) Malignant disease in which, starting with changes in the epithelium of the alveoli and ducts, the basement membrane is perforated and the epithelial cells spread out into the connective tissue of the breast and into the lymphatic spaces, whence they travel by the lymphatics beyond the breast. The surgical treatment necessarily involves removal beyond the limits to which the epithelial cells have spread out.

All the difficulty of the question is concerned with the second category. There is no need for an elaborate terminology concerning malignant disease. Granted that epithelial cells have got out beyond the limits of the basement membrane confining them, there is but one method of treatment. Moreover attempts at prognosis are utterly unreliable when applied to individual cases. It is doubtless true to say that cancers occurring during lactation are excessively malignant and that the atrophic scirrhus in an old woman may never be the cause of her death. Yet there are individual cases which after removal prove exceptions to the general rule. And as to the other names applied to cancer, they have little value, and prognosis based on them is as often wrong as right.

MacCarty distinguished the essential changes which occur in the epithelial cells of the alveoli and ducts into:

(*a*) Primary hyperplasia. An inner row of secreting cells are renewed by the outer row or stratum germinativum. But these cells quickly undergo degeneration. Débris may block the ducts and the alveoli then become dilated; also necrosis between alveoli causes communications and so cystic formations are produced. At the same time there may be a leucocytic infiltration of the connective tissue around the alveoli.

(*b*) Secondary hyperplasia. Not only the cells of the stratum germinativum, but also the cells formed from that layer take part in the proliferation. There is no longer any differentiation between the cells of the outer and inner layers. Malignancy threatens, e. g. in the case termed cystic adenoma.

(*c*) Tertiary hyperplasia. In this cells originating from the stratum germinativum penetrate the basement membrane and migrate into the tissue outside the alveoli.

There is really no difference in appearance between the epithelial cells in the two latter categories. This fact is of first importance when no idea can be formed as to any differences in causation. The general conclusion must be that when any one of these varieties of hyperplasia of the epithelium is noted, removal is indicated.

The question of the removal of all rather than a part of the breast is related to the need for a more thorough histological examination. Lenthal Cheatle demonstrated the advantage of examining large sections as compared with the customary plan of examining a section or two from the part of the breast which appears most diseased to the naked eye. It would involve a laborious examination, but if 100 consecutive specimens of breasts removed because affected by supposed benign growth could be examined by making serial sections, and each section be separately and thoroughly examined both by the naked eye and by the microscope, much light would be thrown upon this moot question. Even by partial steps in this direction minute nodules may be found differing from the main disease, an island of what has been termed above tertiary hyperplasia, amongst structures showing only secondary hyperplasia. Such isolated areas of malignancy explain why in some cases after the removal of the breast for a presumably benign growth, cancer has appeared in the axillary glands. Attempts have been made to distinguish changes limited to the ducts, the so-called duct papilloma, but Cheatle's large sections showed that it was difficult to draw a line of demarcation between proliferation of the epithelium of the ducts and that of the epithelium of the alveoli.

The confusion produced by the terminology in use is marked in the case of the two commonest expressions fibroadenoma and chronic cystic mastitis. The term fibroadenoma may be applied to an inflammatory swelling the result of a congenital or acquired obstruction to a secondary duct of a lobule, and which is followed by retention in the alveoli of the lobule. This excites an inflammatory formation of fibrous tissue around the alveoli of the lobule. Such a swelling may be purely local, the rest of the breast remaining sound, and there is therefore no need to remove the whole breast. On the other hand, the term may be applied to a tumour which commences as an epithelial proliferation within the alveoli, which then gives rise to obstruction, retention, and inflammatory formation around. But the essential fact is the epithelial proliferation, about which there is entire ignorance as to causation, but a probability that other parts of the breast are similarly affected. Then amputation of the whole of the breast is required. The name chronic cystic mastitis suggests inflammation and treatment short of excision, but it is commonly applied to a condition which originates as an epithelial proliferation, described above as secondary hyperplasia. Müller described 14 cases of 'chronic cystic mastitis' in women, all over 30, and rightly concluded that the whole breast should be amputated. In France it is often called Reclus Disease, and Cumston recognized it as essentially an epithelial growth, for the time being benign, for which amputation of the whole breast is necessary.

Greenough and Simmons discussed the cases included under the intentionally vague term of cystic disease of the breast and the misleading one of chronic cystic mastitis. They found that cancer was reported to follow in 10–25 per cent. Among the 83 cases they referred to, there were evidently included not only the changes above described as secondary hyperplasia, but also some with tertiary hyperplasia, and perhaps some which were inflammatory without epithelial proliferation.

In America the removal of the breast. leaving the nipple and overlying skin, has been practised largely since J. Collins Warren recommended it in 1897. By means of a curved incision below and to the outer side, the breast was turned up from off the pectoral muscle: it was then cut away, leaving the skin, subcutaneous fat, and nipple.

Of the 83 cases, in some only part of the breast was removed, and in 8 there was a progressive development of the disease in the remainder. In 5 cases a similar disease developed in the opposite breast. In 3 cases cancer supervened after a complete Warren's operation and in 1 after partial removal.

A single woman aged 33 had a cyst removed the size of half a lemon surrounded by a thick fibrous wall. 3 years later she presented an inoperable ulcerating tumour of the breast and a large malignant mass of enlarged glands in the axilla.

A single woman aged 22 had indurated fibrocystic areas in the left breast, and a similar less marked state in the right breast. A year later a large mass occupied the upper half of the left breast, side of the chest, axilla, and infraclavicular region. The condition was inoperable, but a specimen was removed for microscopic examination and proved cancerous.

A woman aged 42 had a small cystic mass which had been noticed for 3 months. The breast removed by Warren's operation exhibited marked epithelial proliferation, papillary and adenomatous. Three years later there was recurrence in the breast and axilla, when the complete operation for cancer was done, and two years after there had been no further recurrence.

A woman aged 42 had diffuse induration of the left breast which had existed for six months. A partial Warren's operation was done and papillary and epithelial proliferation noted on microscopic examination. Six months later there was a blood-stained discharge from the nipple, but further operation was refused. Eight years later the patient was still alive, but with cancer infiltrating both breasts, both axillae, the clavicle, sternum, pleura, and spina.

It is obvious that a consideration of the above cases supports the conclusions that examination of the breast by whole serial sections is desirable, that the essential distinction which should be made is between an epithelial proliferation which nowhere has migrated outside of the basement membranes, and any instances of epithelial cells invading the stroma of the breast should indicate the necessity for the complete operation for cancer. One of the cases aged 22, shows that the age of 30 often taken represents merely an average and should be controlled by the results of a microscopic examination.

It seems very doubtful whether Warren's method of leaving the nipple and the skin around the nipple has really any advantage. It is suggested that if the nipple be left on, the skin may be stuffed out by a transplantation of subcutaneous fat. It would seem much safer to amputate the breast by the eliptical incision which includes the nipple and an oval area of skin.

Another instance of the unsatisfactory character of the present terminology from a practical point of view is that of 'Paget's Disease of the Nipple'. In his lectures on surgical pathology Paget distinguished a series of scirrhous cancers deviating from the usual in which the nipple and skin are peculiarly affected. Commonly the scirrhous cancer extends from the mammary gland to the nipple and areola. But the changes may commence and predominate in the nipple and areola. There may occur a superficial ulcer like an irregular excoriation whilst the structures of the gland are yet healthy. The term came to be generally applied to an intractable form of eczema and ulceration around the nipple which after lasting for years ended in squamous-celled carcinoma.

Sampson Handley has attached Paget's name to the first of the two conditions noted by Paget, a slowly progressive form of cancer spreading out by way of the ducts to the nipple and thence in a circular area over the skin of the breast.

Jopson and Speese at the Mayo Clinic noted the following conditions which are likely from the clinical standpoint to be called by Paget's name. Inflammation affecting the cells of the rete malpighii followed by spheroidal-celled carcinoma spreading out from the gland by way of the ducts; a similar inflammation, so-called simple eczema, also a simple eczematous ulceration, which may in the end be followed by squamous-celled carcinoma; this last is very rare as compared with the spheroidal-celled carcinoma.

Instead of using Paget's name a microscopic examination of a small piece is the essential step. Simple eczema has been cured, amongst other ways, by X-rays. However slow has been this progress, if cancer is found, the complete operation is required.

Cancer of the Breast. In addition to observations made above, the following suggest themselves after reading recent communications on the subject. The cancer spreads from its point of origin in ring-shaped fashion, in the breast, in the skin overlying the breast, and in the deep fascia. The next extension is by way of the lymphatics to the axillary glands. Subsequent extension to the supraclavicular glands, the skin of the axilla and the chest wall render the case inoperable. Then the Hippocratic aphorism still has an application: 'Treated they die quickly, not treated they may last a long while'. No success has attended the removal of glands above the clavicle. The excision should not include the removal of skin from the armpit. In operable cases it is unnecessary and tends to bind down the arm; it is an important part of the operation to ensure that the patient shall afterwards be able, without difficulty, to raise her hand to the back of her head. Oedema of the corresponding arm or hand is also a contra-indication to operation.

When the complete operation is done on an early and apparently favourable case, then if metastases supervene the scar of the operation and the axilla remain free from recurrence, the metastases appear in the bones, in the sternum, spine, humerus, femur, or frontal bone, also in the opposite breast. This last instance may be a fresh appearance of cancer altogether. A metastasis in the liver is usually later in appearance. In cases regarded as favourable for operation there does not appear to be a tendency to spread directly by the thoracic and abdominal wall to the liver. Were it so, the first metastatic appearance should be in the liver. Metastatic formations in the liver are generally later, whether the primary disease has been treated or not, and there can be no doubt that then the invasion is by way of the blood-stream. Thus the proposal to remove deep fascia as far down as over the head of the rectus abdominis lacks support.

There is a general agreement that harm is done by cutting out a piece for microscopic examination before the main operation. The better arrangement is for a microscopic examination in the course of the operation.

Judd recorded the results obtained at the Mayo Clinic between 1902 and 1912.

Total cases 609. 607 females. 2 males.
Results known in 514.
  266 known to be dead.
    3 died soon. (1) Pulmonary embolism, two weeks after the wound had healed.
      (2) Diabetic coma 4 weeks after.
      (3) Septic phlebitis 4 weeks after.
    2 died of other causes than recurrence.
  242 died of recurrence.
  248 survived over two years, but 37 had recurrence.

The survivors over 3 years were 44·7 per cent. of the total number.

4 cases illustrated the uncertainty of grounding a prognosis on age:

(1) aged 26 was alive without recurrence $7\frac{3}{4}$ years after operation.
(2) aged 25 was alive without recurrence 6 years after operation.
(3) aged 26 was alive $2\frac{3}{4}$ years after operation and perhaps had recurrence.
(4) aged 28 was alive without recurrence $2\frac{3}{4}$ years after operation.

Instances of late recurrence 9 years, 5 years 11 months, 6 years 4 months, 6 years 5 months, one case recurred after 12 years and was well 3 years after a second operation.

Rodman stated that of 50 consecutive private cases 36 (72 per cent.) were alive 3 years after operation: 13 were dead, and 1 was dying of recurrence. This marks the highest level of success. 7 had passed the 10-year limit from the operation, 24 the 5-year limit, 30 the 4-year limit.

Armstrong of Montreal stated that of 82 cases of cancer 33 (40 per cent.) were alive over 3 years from the operation.

Borelius of Lund, Sweden, between 1898 and 1908 did 138 operations for cancer of the breast, one patient died from heart failure. 77 cases were heard of, of which 27 (35 per cent.) survived and were free from recurrence after three years. 50 died of recurrence.

Between 1909 and 1915 there were 212 operations of which the result was known in 198. There was one death from pulmonary embolism. Of the 198, 63 (31·8 per cent.) were free from recurrence after 3 years, and 135 had recurred.

There were besides 7 instances of late recurrence from 3–10 years.

Willy Meyer among 125 cases between 1894 and 1916 had a successful result in between 30 and 40 per cent.

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W. G. S.

TRAUMATIC ASCENDING NEURITIS

Although this condition has been diagnosed clinically for many years, its pathology remains obscure, and even its existence has been disputed. It seems to have been most widely accepted in France, and although several small series of cases have been reported from Germany, Oppenheim, Strümpell, and others express doubts as to its occurrence. It has hardly figured in the literature of this country at all, though Gowers gives a passing mention to it in his text-book.

Of recent years considerable light has been thrown upon the process of ascending neural and perineural infection and intoxication by Homen, Marie and Morax, Meyer and Ransom, by Orr and Rows, and more recently by Teale and Embleton in this country. It seems clear, however, that both clinically and pathologically, the syndrome known as ascending neuritis is quite distinct from the ascending perineural lymphogenous toxi-infections.

One of the earliest cases was described in 1861 by Remak. It appears to have been typical of the condition. Three months before coming under observation, the patient had driven a splinter beneath the nail of his little finger. The injury had taken a fortnight to heal. When seen by Remak there was painful swelling of the ulnar nerve, with cramps, wasting and weakness of muscles supplied by the nerve. Remak regarded it as a case of infection of the nerve endings which had spread up along the lymph channels of the nerve.

In 1896 Kausch described a good case in which following a wound of the middle finger an ascending neuritis of the musculospiral nerve had developed. In this year, also, Krehl described several cases in Germany.

In their text-book, Remak and Flatau (1900) describe the condition as being rare, and attribute it to direct infection of the nerve endings in a wound.

G. Bolten (1908) reviews the published cases and adds five of his own. He distinguishes an ascending perineuritis as well as a neuritis. Both follow small wounds of the hand or fingers. In the former, subjective changes predominate, such as pain and hyperaesthesia. There are some trophic changes; glossy skin or cyanosis of the affected extremity, but no marked weakness or wasting, nor sensory loss. In ascending parenchymatous neuritis, on the other hand, there are wasting and sensory loss as well as subjective disturbances. Finally, joint disorders may result from immobilization. The nerve innervating the region of the injury may be swollen and tender in its course, while in some cases symptoms are referable to the whole brachial plexus.

K. Mendel in 1909 published a series of eight similar cases.

In France, Déjerine and Sicard have given the most comprehensive descriptions of the condition, while the single recorded pathological examination was made by Déjerine and André-Thomas.

From these several sources a general idea of the clinical aspect of the condition may be obtained. The **cause** is generally a trivial injury to the pulp of a digit, though other parts of the hand may be the seat of the lesion. Except in one or two isolated cases there has been a small wound of the skin, such as a scratch, a prick of a pin, of a thorn, or of a splinter. There is usually delayed healing, though evidence of infection is not always obtainable. This is probably because the original trivial wound has healed before the patient comes under observation for nervous symptoms. However, in a case reported by Leenhardt and Norero, the injury was simply a sprain of the thumb sustained in a fight, while Walshe has also recorded a similar case following a blow on the heelcap of a boot without any direct injury of the skin.

It is remarkable that in almost every instance it is the upper limb which is affected, while the injury is always comparatively trivial. The **symptoms** begin with severe pain in the injured digit, radiating up the limb and rendering all movements so distressing as to disable the limb. In fact, it is said that the patient's life may ultimately be rendered burdensome from the continual burning and radiating pain. Simultaneously the pulp of the digit atrophies, the finger becomes tapering and covered by a glossy, atrophic, and cyanosed skin. The digital joints become fixed, and the condition may ultimately involve the whole hand, which becomes oedematous.

The degree of actual wasting and paresis of muscles varies, but in long-standing cases it may be extreme. Objective sensory loss is exceptional, but intense hyperaesthesia may be found in association with the pain. The nerve-trunks and often the whole brachial plexus are very tender to pressure. Ultimately widespread fixation of the joints of the limb, and extensive oedema may result. The more severe cases tend slowly to progress, but in mild cases, recovery may take place in three or four months. It is not clear whether treatment has any definite modifying effect upon the course of the process.

During the period of the war Guillain and Barré, and Ferry have recorded fresh cases corresponding to the condition described above. Walshe has recorded four cases somewhat like these, in which, however, objective symptoms predominated, while pain, hyperaesthesia, and trophic changes were not a marked feature.

All his cases involved the lower limb: three followed superficial gunshot wounds over the peripheral endings of the nerve subsequently affected, while in the fourth case the clinical picture of a severe ascending neuritis of the sciatic nerve followed the blow of a spent bullet on the iron heelcap of the boot. The features of these four cases were (1) muscular wasting and atrophy with sensory loss corresponding to the distribution of a single peripheral nerve, (2) loss of the corresponding tendon jerk, (3) the symptoms were within the cutaneous territory of the nerve endings involved in the injury. (4) There was no traumatic lesion of the nerve-trunk.

The **Pathology** of ascending neuritis is quite obscure. On a case described by Aynaud in 1907, Déjerine and André-Thomas later obtained an autopsy. Unfortunately, the patient had tabes dorsalis ('tabes fruste') also, and this prevented any examination of the cord. Clinically, the case was one of ascending neuritis of the median nerve following a pinprick of the thumb. Vasomotor, trophic, and subjective sensory phenomena were present, and ultimately the limb became fixed in a position of half flexion, adduction, and pronation. The fingers were all completely flexed, but the thumb was abducted and extended. The skin of the hand was shiny and atrophic, and the finger-nails coarse and curved. Extreme pain was produced by any attempt at passive movement, there was constant pain in the thumb, and the nerve-trunk and the brachial plexus were tender to pressure. There was slight atrophy of the small hand muscles.

Post mortem, the median nerve was normal in appearance. The digita cutaneous branches to the thumb and to the radial side of the index were completely degenerated. There was degeneration in some of the terminal branches of the radial nerve on the back of the hand. The distal half of the median nerve showed marked fibre degeneration. The ulnar nerve was practically normal. This degeneration was confined to cutaneous fibres, and the muscular branches of the nerve were normal. The degeneration could be traced upwards into the 6th and 7th cervical dorsal roots, which were shrunken and degenerated. The corresponding dorsal root ganglia were also extensively degenerated. The changes of tabes in the cord itself prevented further investigation. There appears to have been no signs of inflammatory interstitial reaction in the nerve, and the lesion can best be described as a selective degeneration of afferent fibres arising in the neighbourhood of the original injury.

Déjerine and Thomas find themselves unable to explain the nerve lesion, which it seems scarcely justifiable to call a neuritis.

Guillain has compared the process underlying 'ascending neuritis' with that occurring in tetanus and other known ascending neural processes.

But from a study of the work of Orr and Rows it seems clear that this is not a fair analogy. In the ascending perineural lymphogenous infections, the organism ascends by the perineural lymphatics, and there may be an inflammatory reaction in and around these channels. The nerve elements are usually not affected, nor are the symptoms of an ascending neuritis present. Moreover, when clinical symptoms referable to the distribution of the conducting nerve do appear, it is probable that they are of central origin and dependent upon a lesion of the spinal or cranial segment with which the nerve is connected. From a clinical study of extra-faucial diphtheria, Walshe has suggested that the initial paralytic symptoms in diphtheria are due to such a perineural conduction of the toxin to the central nervous system, and there is some evidence that these paralytic phenomena are of central and not of peripheral origin.

In other words, in these ascending infections and intoxications we are not dealing with an ascending neuritis, but with the conduction upwards of noxious substances in lymph channels. The recent work of Teale and Emblĕton has brought tetanus into line with the other infections in this respect, and it seems probable that tetanus toxin ascends by the same path as other toxins, and not exclusively by the axis cylinders as has been thought.

It may be stated, therefore, that clinically 'ascending neuritis' differs somewhat from the familiar forms of neuritis, while the one recorded case in which the lesion could be examined does not altogether confirm the view that the process is such a neuritis as direct infection of the nerve endings might be expected to produce.

Another explanation has been put forward for these cases, presumably on the principle of explaining the obscure by invoking the unknown, and that is to call them cases of 'reflex paralysis'. The best-known form of reflex paralysis, and the most widely accepted, is that which follows an acute arthritis. In this muscles, usually the extensors, proximal to the affected joint rapidly waste. The weakness depends upon the degree of atrophy, and the corresponding tendon jerk is normal or increased unless the wasting is profound. Sensory and trophic changes are absent. It is indicative of our ignorance of the origin and nature of both reflex and ascending paralyses that usually when a case is presented as the one, someone can be found to say that it is the other. It is not surprising, therefore, that we find such experienced clinical observers as Oppenheim expressing doubt as to the existence of such a condition, and declaring that most of the cases he has seen have proved to be cases of hysterical paralysis and spasm. Whatever be its pathology, the clinical condition described by French writers as 'la névrite ascendante' and by German writers as 'Neuritis ascendens' or 'Neuritis migrans', which follows trivial injuries to the hand and fingers is exceedingly rare; indeed less than a dozen cases seem to have been recorded during the past five years.

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F. M. R. W.

ABSTRACTS

SURGERY

Nicolayson, A. Volvulus Coesi. [**Volvulus of the caecum.**] *Med. Rev.*, 1919, **36**, 503–28.

Nicolayson gives a detailed account of two cases of volvulus of the caecum, both of which terminated fatally at the Communal Hospital in Bergen. After discussing this condition, its causes, symptoms, treatment, &c., he reviews the results achieved by various operations and by expectant treatment, as shown by the records of 91 published cases. It is strange to find as many as 30 of these cases hailing from Finland alone, and within as short a period as 5 years. Yet he has drawn on English and German, as well as on Scandinavian sources. Of the 91 patients, 33 recovered and 58 died. All the 7 patients on whom no operation was performed died. Of the 17 patients who were operated on, but whose torsion of the caecum was either overlooked or was found, but not corrected, 15 died. The 2 survivors were left with fistulae of the gut. Of the 66 cases in which detorsion was successfully effected, 31 terminated in recovery, 35 in death. The results of various operations are tabulated thus:—

	Total Number	Recoveries.		Deaths.	
		No.	%	No.	%
Detorsion only	30	18	60	12	40
Detorsion and puncture of caecum	9	7	78	2	22
Detorsion and intestinal fistula	13	3	23	10	77
Detorsion and entero-anastomosis	2	1	—	1	—
Detorsion and resection	9	2	22	7	78

Hernia appeared to be a grave complication; it was present in 9 cases, all but 2 of which terminated fatally. Nicolayson points out that though his statistics suggest that the simplest operations are the best, his figures are too small to be conclusive. Besides, the cases in which entero-anastomosis or resection was performed were probably more serious before operation than those in which detorsion, with or without puncture of the caecum, was performed. C. L.

Andersen, K. Universel mesenterial lymfadenit med appendicitlignende sygdomsbillede. [**General mesenteric lymphadenitis simulating appendicitis.**] *Med. Rev.*, 1919, **36**, 528–36.

In the course of about 300 operations for acute or chronic appendicitis, Andersen has in 7 cases failed to find definite lesions of the appendix, but in every case there was enlargement of all the mesenteric glands, with an effusion which was serous in 6 cases, creamy in 1. In 3 cases acute appendicitis had been diagnosed, and in 4 the operation was performed during the (hypothetical) free interval of recurrent appendicitis. He gives details of his cases, the first of which is of peculiar interest as it throws light on that large and heterogeneous group of P. U. O. in childhood. The patient was a girl of 10, who had occasionally complained of pain in the abdomen during the past year. Two days before admission to hospital she became acutely ill, with fever and pain in the lower abdomen. In hospital her temperature was 39° C., her pulse 140. The abdomen was flaccid except on the right side, where there was some muscular rigidity, and where a slightly movable, very tender swelling was demonstrable. There was neither diarrhoea nor vomiting. Acute appendicitis was diagnosed, and laparotomy performed. Fluid, clear as water, escaped from the peritoneal cavity, and every section of intestine inspected was slightly injected. The appendix was not more injected or swollen than other portion of the intestine. The size of the numerous enlarged mesenteric glands ranged from that of an almond to that of a pea, and one of these glands, which was situated in the mesentery of the appendix, was evidently the swelling detected before the operation. Appendectomy was performed, and a gland removed for examination. This showed simple inflammation and no sign of tuberculosis. The appendix showed slight but acute inflammatory changes. The operation wound healed satisfactorily, but the temperature persisted for about two months. Apart from the operative findings, there was nothing to account for it. v. Pirquet's reaction was repeatedly negative, as was Widal's. After the gradual subsidence of the fever, complete recovery followed, and there was no recurrence of the abdominal pain. There was no enlargement of the lymphatic glands in other parts of the body than the mesentery.

In every case in which this condition of the mesenteric glands was found, the gall-bladder, stomach, and (in females) the internal reproductive organs were examined and found normal. In 3 cases v. Pirquet's reaction was repeatedly negative. Yet none of those conditions was present which, in spite of the existence of tuberculosis, render this reaction negative. Andersen, therefore, excludes tuberculosis in these cases. The disease, whatever its origin, exhibited two distinct phases ; either there was an acute general irritation of the peritoneum simulating acute appendicitis, or the symptoms were comparatively mild and indicative of a chronic process. Were the enlargement of the glands confined to the region of the appendix, the disease might be regarded as a direct sequel to appendicitis with frequent, small, acute relapses. But the general distribution of this enlargement can only be accounted for, if the appendix is to be blamed, by one of two hypotheses. Either there is such free anastomosis of the lymphatic system that a retrograde process of infection can occur, or recurrent exacerbations of appendicitis start a series of slight general infections of the peritoneum, leading to absorption of septic matter from the peritoneal cavity to the lymphatics of the mesentery. This hypothesis assumes absorption through stomata on the surface of the visceral peritoneum. There is, however, no anatomical or experimental proof that fluid in the peritoneal cavity can escape through the visceral peritoneum.

The most plausible explanation, in Andersen's opinion, is based on the assumption that this universal involvement of the mesenteric glands is the result of universal infection of the intestinal tract, the appendix included. In other words, microscopic examination of any section of the intestine would show the same changes as found in the appendix. Andersen is convinced that this condition is not very rare: if the mesenteric glands were to be examined at every operation for appendicitis, they would probably be found enlarged in a considerable proportion of cases. In 3 cases the symptoms disappeared after the operation. The removal of the appendix is probably advisable in these cases, for even if the whole intestinal tract is infected, the appendix may yet be the primary focus of disease.

C. L.

Holst, S. F. Bidrag til mammacarcinomernes statistik. [**Results of operations for cancer of the breast.**] *Norsk. Mag. f. Laegevidensk.*, 1920, **81**, 272–90.

Holst's figures deal with 81 women in the period of 1907–16. He classifies them according as (1) there was no sign of metastases in the axilla, as judged by microscopic examination of the glands, (2) there were metastases in the axilla of the same side, with, however, a prospect of recovery after a radical operation, (3) the disease was more advanced, the patient being discharged without an operation, or undergoing an operation with only a palliative object. As judged by an observation period of 3 years or more, 28·6 per cent. of the cases operated on showed no sign of relapse. Of the 21 patients in the first class, 66·7 per cent. showed no sign of relapse after 3 years. Other points of interest were the following: In 6·3 per cent. there was a history of trauma, occurring 14 days to 3 months before the tumour was detected. The proportion of married women was 77·5 per cent., and of the patients who had given birth, 44·9 per cent. had suffered from mastitis. Holst expresses amazement at the indifference shown by most of the patients to swellings of the breast; the average lapse of time between their detection and the operation was 10 months and 12 days.

C. L.

Neel, A. V. Ti Tilfälde af Lidelse af Nervus ulnaris opstaaet indtil over 50 Aar efter en i Barnealderen paadraget Läsion af Albuleddet. Arthritis deform. traumat. sequel. [**Injury to the elbow in childhood; arthritis deformans in old age. Ten cases.**] *Hosp.-Tid.*, 1919, **62**, 65–77 and 97–110.

Neel observes that an interval of 50 years or more between an injury to the elbow in childhood and the development of arthritis deformans seems extraordinarily long. To judge by the paucity of such cases in medical publications, the condition would appear to be very rare, even though cases with an interval of less than 50 years be included. He can find records of only 21 cases. Yet he has seen 10, the histories of which were curiously uniform, and he suggests that, were surgeons to seek a history of injury in childhood in every case of arthritis deformans of the elbow in middle and old age, they would agree with him in considering this combination fairly common. He gives details of every case, the first of which is illustrative of most of them.

A workman, aged 60, dislocated his left elbow at the age of 6. The joint had occasionally been painful, but it had not prevented his undertaking heavy work. A year and a half before his admission to hospital, weakness and paraesthesia of the ulnar half of the hand were noted. The hypothenar muscles, the adductor pollicis, and the interosseous muscles were atrophied. The hand was slightly claw-shaped, but all movements were free. Hypaesthesia and hypalgesia were demonstrable in the ulnar half of the hand. Movements about the elbow were limited; flexion to 90°, extension to 160°. The movement of rotation was also limited. The whole joint was enlarged, its bony prominences were rounded off, and on electrical examination the reaction of degeneration was demonstrable in the muscles. The X-rays showed much thickening of the articular portions of the olecranon and radius, with proliferation of bone. The humerus also showed some osteophyte formation. An attempt was made to free the ulnar nerve by operation. It was found encapsuled by new bone above the internal epicondyle. The bone was removed and the nerve dissected out. There was considerable thickening of the perineurium, and the circumference of the nerve was much greater above than below the bony bridge. All the constrictions formed by the fibrous perineurium were divided, and longitudinal incisions were also made in the sheath of the nerve. Several months later the condition was no better than before the operation.

The ages at which his patients first injured their elbows ranged from the second to the seventeenth year. In 5 cases the elbow was in the valgus position. In some cases the immediate effects of accident in childhood were slight, but as a rule it left the joint with some limitation of extension. The interval between the accident and the development of symptoms was about 50 years in five cases, 35 in one, 25 in three, and 10 in one. The patient first notices that something is amiss when he cannot execute some ordinary movement. Thus, one patient noticed that he could not ring his bicycle bell. Another found he could not flex his thumb strongly enough in the act of polishing furniture. One patient was a woman who for 40 years had spent about 10 hours a day basket-making. In such a case it is easy to interpret the disease as occupational. Indeed, the differential diagnosis is not always easy, and in one case the atrophy of the muscles was traced to a medullary lesion, and exploratory laminectomy was performed. Only later, when the changes about the elbow-joint became more pronounced, did the peripheral origin of the disease become evident.

Neel suggests that, though the development of symptoms referable to the ulnar nerve seems to be rapid, the progressive character of the disease is more apparent than real. For once the patient has noticed something amiss, he detects atrophy and other signs which he had previously overlooked. This point should be borne in mind lest a tale of rapid progress of symptoms during a short period be construed by the surgeon into an indication for operative treatment. The disease, as far as it affects the nerve, is an interstitial neuritis. As the first case shows, the temptation to operate is hard to resist; the removal of exostoses compressing the ulnar nerve seems so simple and obvious. But it must be recognized that the ulnar nerve has partially accommodated itself during many years to these morbid changes, and that the removal of exostoses may be followed by cicatrices which may further injure a nerve already much damaged. An operation may not only fail of its object, but may permanently injure the few remaining healthy branches of the nerve. These considerations apply with still greater force to operations not confined to removal of exostoses and adhesions, but aiming at multiple incisions of, and injections into, the sheath of the nerve. Possibly an exception to these objections may be found in the case of comparatively young persons whose symptoms are recent and rapidly progressive in spite of conservative treatment. It is also conceivable that when palpation or the X-rays reveal a single exostosis as the only factor responsible for the symptoms, that an operation may prove beneficial. The treatment Neel advocates is hot-air baths and massage, care being taken to massage the neighbourhood of, but not the nerve itself. When its position cannot be definitely ascertained, and this is often the case, massage about the elbow should not be attempted. Electrical treatment is also indicated both for the nerve and muscles. Neel also recommends injections of strychnin and fibrolysin, but he does not seem to speak on this point with the conviction of personal experience. C. L.

NEUROLOGY

Farquhar Buzzard, E. and **Greenfield, J. G. Lethargic encephalitis; its sequelae and morbid anatomy.** *Brain*, 1919, **42**, 305.

This paper, based upon the authors' experience, is an authoritative summary of our present knowledge of this disease.

They state that experience has broadened our outlook on the clinical picture of lethargic encephalitis. We realize now that this varies with the incidence of the inflammatory process on different parts of the central nervous system. It is not astonishing that the symptoms of an inflammation of the brain should vary. An organ with functions so complex and numerous would be expected to give rise to a versatile symptomatology. The diagnosis, therefore, of lethargic encephalitis can never depend upon the presence or absence of any symptom or group of symptoms. It must be determined by a consideration of the onset and course of the disease, and by the elimination of other pathological conditions which may produce similar symptoms and physical signs.

It is possible to group cases into three classes dependent upon the chief incidence of the inflammatory process.

(1) Cases characterized by hemiplegia, hemianaesthesia, and hemianopia.

(2) Cases characterized by symptoms like those of paralysis agitans; the basal ganglia group.

(3) Cases characterized by disturbances of function of the cranial nerves.

In every instance, however, the disease is always more widespread than might be suspected from the most prominent symptoms.

Some of the more severe non-fatal cases are overtaken, after the acute stage of the disease has passed, by more or less disabling sequels. The most common of these is the development of **involuntary movements** of the tongue, jaw, or limbs. These movements are irregular and choreiform in some instances, in others they are of the tremor variety. They tend to cease during the performance of voluntary movements, and during sleep, so that while they do not markedly interfere with voluntary activities they disturb the patient's peacefulness while at rest.

It is difficult to correlate these phenomena with any local lesion, and Buzzard and Greenfield favour the view that they represent the release of some nervous activity by interference with control, rather than a chronic irritative lesion. The fact that they are subject to voluntary control is in favour of this view. So far as treatment is concerned they have found massage, electricity, and drugs equally ineffective, and they rely mainly upon re-educative exercises to produce improvement.

Perhaps the type presenting the greatest difficulties in diagnosis is that of **febrile hemiplegia of subacute onset.** In cases of this character, hemiplegia, hemianaesthesia, hemianopia, aphasia, convulsions, stupor, and even some oedema of the optic disks may be seen. Four very interesting cases of this type occurring in adults of over 40 years of age indicate the difficulty a differential diagnosis between cerebral haemorrhage, thrombosis, tumour, or abscess may present. In two of these cases a decompression was performed. In both great increase of intracranial tension was found. On the surface of the brain were small recent clots, and in one case a quantity of dark fluid blood. Some of the cortical veins were thrombosed and the cortex was hyperaemic and altered in colour. They find that the naked eye post-mortem changes are not sufficient to distinguish between ordinary cerebral haemorrhage and a haemorrhage supervening in the course of an encephalitis.

Histological findings. The histological appearances vary according to the intervals between the onset of the symptoms and the fatal termination. The features common to all cases are summarized as follows:

(1) Vascular congestion.

(2) Evidence of toxic degeneration of the nerve cells and neuronophagy.

(3) Proliferation of the mesoblastic cells of the vessel walls and infiltration of the nervous tissue with these cells.

(4) Small celled infiltration of the Virchow-Robin space.

(5) Glial proliferation.

These changes are given in the order in which they occur most constantly. Other frequent changes are cortical venous thrombosis and small haemorrhages.

F. M. R. W.

Burton Clelland, J. and **Campbell, A. W.** **The Australian epidemic of acute encephalo-myelitis: a consideration of the lesion.** *J. Nerv. and Ment. Dis.*, 1920, **51**, 137.

At the end of the hot dry summer seasons of 1917 and 1918 an outbreak of a peculiar form of acute encephalo-myelitis appeared in New South Wales and in the neighbouring States. It presented the following characters: (1) Acute onset, with a mortality of 70 per cent. Symptoms of cerebrospinal irritation including pyrexia, coma, convulsions, and rigidity, but no paralysis. Occasionally an ocular nerve palsy or a monoplegia was seen and sometimes followed by paresis 'such as so frequently follows acute poliomyelitis'. (2) The outstanding nervous lesion was a perivascular lymphocytic infiltration distributed throughout brain and cord, but most severe in the corpus striatum, pons, and medulla. (3) The disease was transmitted successfully to monkeys by intracerebral inoculation. Intense inco-ordination was the predominant clinical feature of the disease as it affected these animals. From infected monkeys the disease was carried over to sheep, and from these back again to the monkey. It was also conveyed to a horse and a calf. Of the series of sheep inoculated some were unaffected, others showed slight symptoms suggesting an encephalo-myelitis, while others died from the disease.

The authors regard the disease as differing clinically from acute polio-encephalo-myelitis. They think that its virtue may be a mutant, breeding relatively true, of the virus of acute poliomyelitis, or it may be a distinct species of organism. Between these alternatives they are unable to decide.

Dealing with the lesion they state that the round-celled infiltration was the earliest visible change. They argue that this lesion, whenever occurring, is due to mechanical irritation from the presence of the bodies of the organisms concerned in the vessels, or it may be a reaction to circulating toxins produced by organisms elsewhere in the body. They adopt the latter explanation for the cases under discussion, though they cannot exclude the presence of organisms in the vessels. Such nerve-cell changes as they found they regard as purely secondary to the vascular lesion, and they attribute all the symptoms to the mechanical and physiological effects of the cellular reaction round the vessels. From this they argue that the limited case incidence of the malady in an epidemic depends largely upon the fact that in some individuals there is no cellular reaction in the nervous system, and hence they do not develop the symptoms of the disease. In others there is an intense reaction which interferes with function and so causes death. The response of an individual to infection may be modified unfavourably by such external factors as exposure to severe heat, or head injuries.

F. M. R. W.

Guillain, G. et **Barré, J. A.** (1). Le Réflexe Tibio-fémoral postérieur. [**The posterior tibio-femoral reflex.**] *Bull. et mém. Soc. méd. d. hôp. de Par.*, 1917, **33**, 284. (*Rev. neurol.*, 1917, i, 335.)

Guillain, G. et **Barré, J. A.** (2). Le Réflexe Péronéo-fémoral postérieur. [**The posterior peroneo-femoral reflex.**] *Bull. et mém. Soc. méd. d. hôp. de Par.*, 1917, **33**, 287. (*Rev. neurol.*, 1917, i, 336.)

The tibio-femoral reflex is the tendon jerk obtainable by percussion of the tendons of semitendinosus and semimembranosus. To elicit this, the leg is abducted and rotated out, the hip and knee are moderately flexed. The contraction can be seen and felt. Its segmental representation is 4th and 5th lumbar, and 1st sacral segments.

The peroneo-femoral reflex is the tendon jerk obtainable by percussion of the tendon of biceps femoris. The patient lies on the opposite side with the leg flexed.

It is obtainable under the same conditions as other tendon jerks, and is modified by disease as these are. Thus they are absent in tabes dorsalis and may be absent or diminished in sciatica. They are exaggerated in spastic conditions.

Both these tendon reflexes have been described by Walshe (vide *Brain*, 1914, **37**, 275) as 'the hamstring jerks'. They are most readily obtained with the limbs in the postures described above. The index finger is then laid across the tendons at their insertion and percussed. In this way the contraction can be felt even when it is not visible, as is the case in well-covered women, while in these circumstances the tendon can be accurately hit off more easily by this method. The semitendinosus-semimembranosus jerk is usually more easy to obtain than the biceps jerk, and the investigation of the former serves all practical purposes. In spastic paralysis the hamstring jerks are very facile, and in the form of paraplegia-in-flexion they remain active even when, as is often the case, the knee and ankle jerks are abolished.

F. M. R. W.

Friedman, E. D. On a possible significance of the Babinski and other pathologic reflexes. *J. Nerv. and Ment. Dis.*, 1920, **51**, 146.

Friedman revives a view much favoured in recent years by continental neurologists to explain the various reflex phenomena seen clinically after lesions of the pyramidal system. The view in question is based upon phylogenetic considerations, and refers these reflex reactions to atavistic manifestations of the movements of our supposed arboreal ancestors.

Friedman, in the present instance, explains the Babinski plantar reflex as a reappearance of the prehensile hallux functions of the tree-climbing monkey. In general this way of looking at clinical phenomena has the disadvantage of being capable neither of proof nor of disproof, while in its present application it seems reasonable to say that the close clinical study of the reflex in question in France and in this country has rendered any such speculative hypothesis superfluous. Nor is the idea so original as Friedman supposes, for an identical suggestion was put forward in 1912 by van Woerkom (*Rev. neurol.* ii, 285).

Further, in developing his thesis Friedman appears to have fallen into at least two cardinal errors. He accepts the anatomical nomenclature of the dorsiflexors of the foot and toes as physiological evidence that they belong to the extensor group of muscles of the limb. There is now abundant evidence both physiological and clinical for regarding the dorsiflexors as belonging to and acting with the lower limb flexors. The mere fact that these muscles have been named extensors is not, therefore, reason for separating the Babinski response from the flexion or withdrawal reflex of the limb. In fact, it seems reasonably certain that the former is but a part, and an integral part, of the flexion reflex.

Equally inaccurate is his suggestion that this reflex is due to abolition of reciprocal innervation. Not only is such a view incompatible with its reflex origin and nature, but clinical examination, in the light of Sherrington's work, has established that reciprocal innervation does obtain here. Thus, a knee clonus (an extensor reaction) is abolished by the occurrence of a flexion reflex, even when this is not of sufficient amplitude to flex the knee (*Brain*, 1914, **37**, 269).

This paper is an example of pure speculation founded not upon careful clinical work, but upon the extraction from neurological literature and the marshalling into an argument of anything that appears to bear out the writer's preconceived notions: the general purport of the writings quoted and any discordant facts they contain being totally disregarded.

F. M. R. W.

Brouwer, B. The significance of phylogenetic and ontogenetic studies for the neuropathologist. *J. Nerv. and Ment. Dis.*, 1920, **51**, 113.

In a most interesting paper Brouwer emphasises the importance of phylogenetic and ontogenetic studies for the appreciation of clinical and pathological findings in neurology. Taking disseminated sclerosis as a text he points out the frequent discrepancy between the severity and the character of the clinical symptoms and the pathological findings in the nervous system. Although the number and topography of the sclerotic foci vary greatly from case to case, yet the symptomatology of the disease has a fairly uniform character; thus spastic paresis, tremor, dysarthria, and horizontal nystagmus, exaggerated tendon reflexes, Babinski plantar responses and absent abdominal reflexes are practically constantly found. On the other hand, permanent sensory loss is rare, while disturbances of the ocular muscles and of the functions of the sphincters are fleeting and inconstant.

He quotes cases in which the brain-stem and the emerging cranial nerves were thickly sown with foci of disease, but in which cranial nerve palsies were insignificant. Again, the optic nerves may be completely sclerosed, and a simple temporal pallor of the disk may be the sole clinical evidence of the fact. The persistence of the axis cylinders in sclerotic foci affords no explanation of this, since if some functions are spared for this reason, why not others?

Brouwer thinks that the solution may be found by considering the problem from the point of view of evolution, and the hypothesis he puts forward is in essence a restatement of views originally advanced many years ago by Hughlings Jackson.[1] Jackson said that disease of the nervous system might be regarded as a progressive dissolution of the functions of the nervous system; using the word dissolution as the opposite of evolution. The highest, most recently acquired—ontogenetically or phylogenetically—and least deeply organized activities of the nervous system are the most vulnerable and first to be lost; 'there are degrees of loss of the latest acquirements with conservation of the earlier, especially of the inherited acquirements. Speaking of the physical side, there are degrees of loss of function of the least organized nervous arrangements with conservation of function of the more organized. There is in each reduction to a more automatic condition; in each there is dissolution, using this term as Spencer does, as the opposite of evolution'. (*Brain*, 1915, **38**, 107).

As a concrete application of this view, Brouwer cites a case of disseminated sclerosis in which although almost all the cranial nerve nuclei in the brain-stem were involved in patches of disease, yet a gross defect of articulation was the only pronounced clinical manifestation. Articulation being a more recently acquired and a higher expression of function than the simple activities of the other cranial nerves, is disturbed while these escape. Similar examples are given from cases of median nerve paralysis. Jackson's fundamental contribution to the problem is presumably unknown to Brouwer. F. M. R. W.

RAMSAY HUNT. The existence of two distinct physiological systems for the transmission of motor impulses in peripheral nerves. *Brain*, 1918, **41**, 302.

Ramsay Hunt proposes a division of muscular movements into (1) segmental reflex movements, 'which are very primitive', (2) automatic and associated movements, which are under the control of the corpus striatum, and (3) isolated synergic movements of cortical origin.

Automatic and associated movements arise in the corpus striatum and pass down to the lower motor neurone along extrapyramidal paths, while the cortical motor impulses travel by the pyramidal system. Thus there are two principal components in motility: a primitive strio-spinal system subserving automatic and associated movements and a cortico-spinal system. These are anatomically and physiologically distinct, and Ramsay Hunt calls the former the paleokinetic system, and the latter the neokinetic system, since it is a later and a higher product in the evolution of the nervous system. Further, he supposes that the peripheral motor nerve contains fibres of two types subserving the functions of these two systems. He compares them with the 'epicritic' and 'protopathic' fibre systems of Head, adopts Ranson's view that the protopathic fibre is non-medullated, and thinks it probable that the motor fibres of his paleokinetic system are also non-medullated (vide *Medical Science*, 1920, **1**, 628). In support of this suggestion he quotes Boeke's histological observations that the muscle fibre has both a cerebrospinal and a sympathetic fibre innervation, and he elaborates this view in considerable detail, associating neokinetic motility with the activity of the sarcostyles, and the paleokinetic motility with that of the sarcoplasm.

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[1] Croonian Lectures R. C. P. 188.

The data upon which this elaborate and comprehensive hypothesis is based are somewhat disappointing, and to those acquainted with the writings of Hughlings Jackson and of Sherrington, seem capable of other and simpler explanations. It is perhaps to be regretted that Ramsay Hunt had not the inestimable advantage of a more intimate knowledge of this work of the English school, when considering the difficult subject of motor innervation.

He supposes that in the evolution of motor activity reflex movements were first developed, then automatic and associated movements, and finally the voluntary purposive movements of cortical origin.

We are not told what exactly is meant by an automatic movement, and its differentiation from reflex movements must be taken to imply that it is the outcome of some spontaneous activity of the corpus striatum.

Surely, too, associated movements are originally evoked by some isolated co-ordinated motor act apart from which they can have no existence.

The analysis of the reflex reactions of the decerebrate and the spinal animal has shown that the activities ascribed by Ramsay Hunt to the corpus striatum can be carried out reflexly without the aid of this organ.

In support of his views he quotes two cases of musculospiral palsy in which the power of supinator longus in the movement of flexion of the elbow was lost, but in clenching of the fist to order this muscle and the other extensors contracted powerfully. He explains this as follows: clenching the fist belongs to the group of automatic and associated movements, and the striokinetic fibres subserving these had regenerated, and therefore the supinator longus could be stimulated and thrown into action by this motor system. In voluntary flexion of the elbow, on the other hand, we are dealing with an isolated synergic movement of cortical type. The more highly specialized and more vulnerable fibres of the neokinetic system had not regenerated, and hence impulses travelling along this fibre system could not reach the muscle.

It is not easy to see why clenching the fist to order should be regarded as a more primitive form of movement than a voluntary flexing of the elbow under the same conditions; neither of them could be performed without the intervention of the cortico-spinal system, nor is it very illuminating to be told that the movement of grasping should be regarded as a relic of the antics of some tree-climbing ancestor. Surely, no hypothesis of muscular co-ordination requires such imaginative flights as this.

From a purely clinical point of view, also, we may view with doubt the organic, or purely organic, nature of a musculospiral paralysis in which the clenching of the fist is accompanied by a powerful contraction of all the extensor muscles in the forearm. The phenomenon is highly suggestive of a hysterical residual paralysis, or 'metaparalytic psychogenic akinesia', in which inconsistencies of this type might well be encountered. That the electrical reactions of all the muscles concerned were normal is not without significance in this connexion.

Two or three cases of this type form the only direct evidence adduced in support of the thesis contained in this paper. For the rest, it is difficult to discover, among the many facts and arguments drawn from histology, anatomy, and the study of evolution, any evidence of the existence of a double system of peripheral motor innervation.

Boeke's observations on the double innervation of the muscle fibre, though they are scarcely more than histological observations of uncertain significance and the subject of animated controversy, are made the basis of a highly speculative view of the relations of the striatal and the cortical systems with the two components of the muscle fibre. F. M. R. W.

PRIDEAUX, E. Suggestion and suggestibility. *Brain*, 1919, **42**, 291.

Definitions of the term suggestion commonly fall into two groups: (1) **Normal suggestion,** an everyday occurrence of normal life, and (2) **Abnormal suggestion**, which takes place in psychoneurotics and in normal individuals in abnormal circumstances. The mechanism is the same in both cases, and the difference one of degree only; it is the subject that varies. The 'suggestion' understood by Janet, Déjerine, Grasset, and Babinski is the abnormal form.

As a general definition Prideaux gives a modified form of McDougall's widely accepted definition: 'suggestion is a mental process resulting in the acceptance with conviction of a proposition in the absence of logically adequate grounds for its acceptance.'

Suggestibility is the chief factor in the process of suggestion. It is a subjective process, but is not a mere passive receptivity on the part of the subject's mind, but the result of active processes of an affective character proceeding there.

Four different states of suggestibility are given: (1) **Individual**, which is peculiar to the individual and independent of the nature of the suggestion and of the suggestor. It is due to the varying degree in which the egoistic instinctive tendencies are developed and the manner in which the sentiments have become organized to form ideals. (2) **Conditional** suggestibility, which varies in the individual according to circumstances, and depends upon the affective state of the individual at any given time. (3) **Specific** suggestibility, which has reference to a particular set of ideas alone, and depends upon the affective appeal of these to the individual. (4) **Personal** suggestibility, which depends upon the affective relations of the suggestor to the subject.

Suggestion may be accepted, opposed, or merely refused. Prideaux speaks of these as positive, negative, and neutral responses respectively. An idea is accepted because it harmonizes with some pre-formed interest, or sentiment, and because the affective forces involved enable it successfully to oppose all 'contrary forces' and thus to produce conviction. In abnormal suggestion the process is the same, but here the affective forces involved are stronger, and the contrary forces are weaker, so that the individual is unaware of them and has no control over them. This is best seen in persons suffering from hysteria. Hypnosis is an exaggerated form of suggestion.

The object of suggestive treatment is to set in action the right affective forces for the induction of an appropriate suggestibility, which will harmonize with and reinforce the ideas to be suggested so that these may be accepted with conviction. Therefore, the physician begins by trying to produce an effective personal suggestibility in his patient, and then proceeds to play upon the conditional, specific, and individual factors of the patient's suggestibility. A necessary addition may be 'indirect suggestion', which is the use of some form of specific treatment to make the cure appear reasonable in the patient's mind. Prideaux regards hypnosis as unnecessary in most cases, and he concludes that 'of the methods of suggestion treatment there is no question that the method of normal suggestion by explanation and appeals to feelings is the best'. In that the patient relies on the explanation given to him, treatment by suggestion is not ideal, but it has the merit of usefulness. F. M. R. W.

PATHOLOGY AND BACTERIOLOGY

Ganter u. van der Reis. Zur Klinik der Darmkrankheiten. I. Ein Verfahren aus beliebigen Teilen des Darmes Inhalt zu entnehmen. [**A method of obtaining intestinal contents at any level.**] *Deutsche med. Wchnschr.*, 1920, **46**, 236.

The authors describe an ingenious capsule, made partly of brass and soft iron, which can be operated by an electro magnet through the abdominal wall. The apparatus is swallowed, and its course through the alimentary canal can be followed by X-ray examination. At any particular site, material can be obtained for bacteriological or other examination. The exact construction of the apparatus should be followed in the original paper.
W. B.

Morishima, K. Phenol red china blue as an indicator in fermentation tests of bacterial cultures. *J. Infect. Dis.*, 1920, **26**, 43.

In this communication the author recommends an indicator composed of phenol red and china blue. A 1 per cent. solution of china blue in distilled water is prepared, and while the solution is kept hot in a water bath, normal sodium hydroxide solution is added until the blue colour disappears and the solution becomes brown. Usually about 3·5 c.c. of the soda solution are required to decolorize 100 c.c. of the china blue. To the broth or other fluid medium are added 5 c.c. of a 0·02 per cent. solution of phenol red per 100 c.c. of medium, and the reaction is adjusted to the required P_H. Then 1·2 c.c. of the decolorized china blue solution is added to every 100 c.c. of medium, and the medium is sterilized. The medium is almost colourless, If alkali develops during the bacterial growth a pink colour appears. The production of acid causes first a bright green, due to the yellow of the phenol red plus the china blue; later, the green changes to a deep blue. Decolorized china blue may also be added to agar instead of fuchsin in Endo's method. The indicators described above have been extensively used by Teague and Morishima (*vide* p. 279.) W. B.

Bronfenbrenner, J., Schlesinger, M. J., and **Soletsky, D. On methods of isolation and identification of the members of the colon-typhoid group of bacteria. Study of the bactericidal action of C R indicator.** *J. Bact.*, 1920, **5**, 79.

In a study of the fermentation of carbohydrates by members of the colon-typhoid group, Bronfenbrenner had recommended a mixture of china blue and rosolic acid ('C R') which could be added to the medium to permit of a direct reading of the hydrogen-ion concentration during the process of fermentation without necessitating the destruction of the culture. On applying this indicator to certain cultures it was found that it exerted decided inhibitory effects. The present paper contains the results of the examination of 78 different bacteria in the presence of media containing the C R indicator. 43 of the cultures belonged to the typhoid-colon group, the remaining 35 comprising various cocci, Gram-positive spore bearers, *B. proteus, B. cloacae, B. fluorescens,* and *B. alkaligenes.* China blue in the highest concentration used (0·0625 per cent.) had no inhibiting action on the majority of the microbes examined. The growth of *B. acidi lactici* was, however, completely arrested in a medium containing 0·025 per cent. of the dye. Rosolic acid, even in a concentration of 0·005 per cent. was markedly inhibitory on many of the cultures tested, especially those which gave a Gram-positive reaction. Almost all Gram-negative bacteria examined grew readily on a medium containing 25 times the amount of rosolic acid which is inhibitory for Gram-positive bacteria. This apparent selective action of rosolic acid, coupled with its inability to inhibit growth of *B. dysenteriae,* suggests that it would be useful in the preparation of selective media for the isolation of intestinal bacteria. W. B.

Thjøtta, Th. On the bacillus of Morgan No. 1. A metacolon bacillus. *J. Bact.*, 1920, **5**, 67.

The author isolated Morgan's bacillus No. 1 from 9 cases of diarrhoea or dysenteric colitis, two of which ended fatally. Seven of the strains were studied immediately after isolation as well as after a growth on artificial media for over one and a half years. During this time most of them altered their characters. Thus, while only one strain was non-motile when isolated, only one retained its motility at the end of the period of examination. Two strains lost the power of producing gas in glucose, and acquired the property of producing gas in sucrose and mannitol. The strains of Morgan's bacillus were serologically distinct from other pathogenic bacteria of the typhoid-colon group and differed among themselves. The serum of the patients from whom the strains were isolated showed no agglutinating properties on the homologous or heterologous cultures. The author considers that, although Morgan's bacillus No. 1 shows fairly characteristic properties even after a long period of saprophytic growth, it should be ranged alongside the group of 'metacolon' bacteria of Danish authors.

W. B.

Cruickshank, J. A. and **Lafrenais, H. M. Enteric carriers.** *Indian J. M. Research* (*Special Indian Science Congress Number*), 1919, 125.

This paper details the results obtained from 1,886 British soldiers admitted to the Enteric Dépôt at Parel six weeks after their convalescence from enteric group infections. Of these 1,886 cases—

791 had been diagnosed as enteric fever.
633 „ „ „ „ paratyphoid A.
136 „ „ „ „ „ B.
326 „ „ „ „ enteric group.

The method of examining faeces was as follows: the patient was given a purge of senna, podophyllin, and magnesium sulphate at night. The second stool on the following morning was collected, and the whole stool emulsified with ten times its volume of sterile tap-water. A loopful of this, after it had stood for one hour, was plated out on Conradi's medium. Likely colonies were tested with sera and sugars.

Brilliant green enrichment method was tried, but was not found to facilitate the isolation of paratyphoid bacilli.

Every man was examined ten times at four days' interval before discharge.

The total number of carriers detected was 49. Of these—

34 were carrying *B. paratyph. A.*
9 „ „ *B. typhosus.*
6 „ „ *B. paratyph. B.*

47 were faecal carriers and 2 urinary carriers.

The Widal reaction in all chronic (over 6 months) carriers was positive at least in 1 in 40.

The Widal reaction in temporary carriers was very variable.

Tables are given showing details of findings at various dates subsequent to admission. G. T. W.

Liston, W. Glen and **Goré, S. N.** **A simple method for detecting faecal carriers.** *Indian J. M. Research* (*Special Indian Science Congress Number*), 1919, 107.

The essential points in the method described are:

1. Accurate dilutions of a known volume of faecal material are made in saline.
2. Suitable dilutions are 'plated' out on agar slopes or on Conradi or MacConkey plates.
3. Likely colonies are picked off and examined for motility and agglutination with a mixed T. A. B. serum.
4. Further differentiation is obtained by planting in Aschoff's lead acetate glucose agar.

The method is described in sufficient detail as will enable those with no bacteriological training to attempt it. G. T. W.

Sherwood, N. P., Downs, C. M., and **McNaught, J. B. Non-lactose fermenting organisms from the faeces of influenza patients.** *J. Infect. Dis.*, 1920, **26**, 16.

On account of the confusion between typhoid and paratyphoid fevers and influenza in pandemics of the latter disease, the authors undertook a series of examinations of the faeces of 32 patients with 'influenza' during 1918. They found *B. typhosus* in 3 and *B. enteritidis*-like organisms in 17 others, although similar organisms were not found in control cases suffering from mumps, measles, tonsillitis, lobar pneumonia, or surgical diseases. The significance of the *enteritidis*-like organisms is unknown. The occurence of *B. typhosus* was attributed either to the occurrence of influenza in typhoid carriers or to a mistaken diagnosis. The 17 '*enteritidis*' strains seemed to fall into 4 types, 3 being specific and one heterogeneous. There appeared to be no relation between the nature of the stools and the presence of these organisms. W. B.

Fletcher, William. Capsulate mucoid forms of paratyphoid and dysentery bacilli. *J. Roy. Army Med. Corps*, 1920, **34**, 219.

The author, in the course of routine examinations of two chronic *B. paratyphosus* carriers, met with some capsulated bacilli forming mucoid colonies. These bacilli were morphologically unlike *B. paratyphosus*, but in the opinion of the author they are a variety of that organism.

A patient who had contracted paratyphoid in the Eastern Mediterranean in 1916, and who was a chronic carrier, was examined repeatedly. The stools were plated out on Endo's fuchsin-sulphite-agar, and 50–100 per cent. of the colonies which grew were composed of *B. paratyphosus B*. Plating was repeated 116 times. On the 117th examination only 10 per cent. of the colonies proved to be paratyphoid bacilli and a new type of colony appeared. These were large, slimy, and white. The author designates them as 'mucoids'. Similar results were obtained on the next seven examinations covering eleven days, after which the 'mucoids' disappeared and the percentage of paratyphoids again rose to 50 per cent.

When the 'mucoids' were present they balanced approximately the diminution in the number of the paratyphoids.

When these mucoid colonies were subcultured and their biological reactions examined they were found to react in the same way as *B. paratyphosus*. Serologically, when they were first isolated, they were not agglutinated by paratyphoid serum, but they absorbed the agglutinins from such a serum. Eight months later the same organisms were agglutinated slowly in low dilutions. Experiments have been carried out to show that typical paratyphoid bacilli are produced from the mucoid bacilli.

Elaborate care was taken to obtain absolute purity of the mucoids. Daily platings for three weeks produced nothing but mucoid colonies. A series of peptone-water cultures were then made from single colonies and an Endo plate was made daily from each peptone tube. For two days only mucoid colonies grew. Seven out of eight plates made on the third day produced 30–70 per cent. of paratyphoid colonies. These paratyphoids derived from the mucoids were agglutinated up to titre by a paratyphoid serum and absorbed agglutinin from the same serum. The author never obtained the mucoid form from the ordinary form, but the ordinary form could always be obtained from the mucoids. When the mucoids are examined under the microscope they are found to consist of bacilli 1·5 to 2·5 μ in length. Coccoid forms are also numerous. The bacilli appear to lie in a matrix which prevents them lying in contact with one another. The paratyphoid bacilli derived from the mucoids tend to be larger, involution forms are common, and the matrix is absent.

Stained by Benian's 'relief stain' method the mucoids appear to have a capsule, whereas the paratyphoids have none. Capsules cannot be stained by ordinary methods.

Similar results have been obtained from a patient who was a carrier of *B. aertryck*. The mucoid isolated in this case gave all the reactions of *B. aertryck* except the serological reactions.

Bacilli were obtained by plating out from peptone-water cultures, which gave all the reactions of *B. aertryck* including agglutination to titre and absorption of agglutinins from immune serum.

Mucoid bacilli have also been isolated from dysentery carriers, and from one convalescent who was not a proved carrier. Bacilli resembling dysentery bacilli (mannite fermenting) can be obtained by plating out from peptone-water cultures of these mucoid bacilli. These derived bacilli are agglutinated by immune serum, but do not absorb agglutinins. G. T. W.

Teague, O. and **Morishima, K.** **The action of *B. typhosus* on xylose and some of the other less frequently used sugars.** *J. Infect. Dis.*, 1920, **26**, 52.

Although *Bacillus typhosus* is generally regarded as a very stable bacterial species, Weiss, in 1917, pointed out that 6 out of 31 strains tested by him did not produce acid when grown in xylose broth. Four of these also appeared atypical antigenically in that they did not absorb agglutinins which had been produced by the injection of xylose-fermenting strains. It appeared as if this might be matter of practical significance, because the strain 'Rawlings', which has been used on a gigantic scale for the manufacture of typhoid vaccine, belonged to the xylose-negative group. The present research of Teague and Morishima arose in connexion with this question. Working with 126 strains from different sources, they found that whereas 92 per cent. produced acid in xylose broth, 8 per cent. did not at all or only late. The indicators used were phenol red and decolorized china blue, as recommended by Morishima (vide p. 275), or methylene blue eosin of Holt-Harris and Teague. When typhoid cultures that ferment xylose rapidly are inoculated on xylose-china-blue-agar large blue colonies develop in 24 hours while on methylene-blue-eosin xylose plates the colonies hav black centres. Rapidly fermenting xylose strains breed true on subcultivation.

If, however, typhoid cultures which ferment xylose slowly are inoculated on xylose-china blue plates colourless colonies develop during the first 24 hours. On the second day or later, many very small daughter colonies appear within the isolated colonies on the plate and project like nipples or papillae above the surface. Each isolated colony may contain a dozen or more of these daughter colonies and may grow much more luxuriantly than the mother colony, assuming a deep blue colour. On the methylene-blue-eosin xylose plates, the mother colonies are pink while the daughter papillae are black. The appearance presented is strongly suggestive of a contamination. If, however, the large blue or black colonies are transferred to xylose broth, fermentation may occur in 24 hours, the number of xylose fermenters increasing with the sojourn in the broth. If such a broth culture is now plated on xylose agar containing china blue or methylene blue eosin, all the colonies may be blue or black as the case may be, although they sprang from colonies which at first were only able to ferment the xylose slowly. Similar results were obtained on media containing arabinose—a sugar generally considered not to be fermented by *B. typhosus.* Of 117 strains examined, 6 per cent. showed acid production in arabinose and all gave daughter colonies on arabinose plates. By growth in arabinose broth the number of acid fermenters subsequently appearing in arabinose plates could be greatly increased, and finally none showed daughter colonies as was the case before the sojourn in the arabinose broth. Arabinose fermenters occurred among the rapid and slow xylose fermenters alike. There thus appears to be no relation between the development of ferments for xylose or arabinose by different strains of typhoid although these two sugars are chemically closely related. When subcultures which fermented xylose rapidly were obtained from slow xylose fermenters they remained rapid xylose fermenters although kept on agar containing no xylose. They were all agglutinated by typhoid serum. None of the cultures examined produced acid in dulcitol before the fourth day although they showed daughter colonies as in the case of the two sugars above mentioned. An increased or decreased production of the ferments for one of the three substances, xylose, arabinose, or dulcitol, did not affect the production by the culture of ferments for the other substances. Experiments with media containing dextrose, maltose, galactose, salicin, mannitol, or glycerol showed no daughter colonies, although the latter were obtained on rhamnose.

With regard to the concentration of the sugars giving rise to daughter colonies, it was found that although a good crop was obtained with 1·0 per cent. xylose, only very few were obtained on a medium containing 0·04 per cent. of this sugar. Rhamnose, even in a dilution of 0·01 per cent., gave a good daughter colony formation on the fourth day, as likewise did dulcitol. A concentration of 0·25 per cent. of dextrose did not interfere with the production of daughter colonies on an agar containing 1·0 per cent. of xylose although none were observed to be formed in the presence of the latter sugar when 0·5 to 2·0 per cent. of glycerol was added. These observations are of great interest, and are confirmatory of many others of a like character which have accumulated in recent years through the observations of Massini, Twort, Penfold, and particularly Reiner Müller, Baerthlein, and Burri, an admirable critical analysis of whose work has been published by C. Dobell (*J. Genetics*, 1912–13, **2,** 325).

With special reference to typhoid the published records to date indicate the occurrence of several typhoid 'variants' viz. (1) *B. metatyphi* (Mandelbaum, 1907, 1912), a non-fermenter of glycerine although in contact with this alcohol it reverts to *B. typhosus*; (2) *B. typhi mutabile* (K. A. Jacobsen, 1910), the growth of which is inhibited on autoclaved nutrient agar although it ultimately reverts to the classical type; (3) non-fermenters of xylose (Weiss, 1917), which according to the present authors are really slow fermenters which revert to the common type, and (4) artificially produced variants (Teague and Morishima, 1920), including rapid arabinose and rapid dulcite fermenters. Two other variants are also referred to, viz. strains which when freshly isolated are inagglutinable, and the so-called 'blue typhoids' which produce a deep blue colour in litmus milk early (third to sixth day), and retain this property. Since, however, these variants all revert to type and are agglutinated by typhoid serum, Teague and Morishima would seem to be logical in stating they 'cannot be allowed to alter the conception of *B. typhosus* as a homogeneous organism'. W. B.

Kendall, A. I., Day, A. A., and **Walker, A. W.** (1). **The metabolism of virulent human tubercle bacilli.** *J. Infect. Dis.*, 1920, **26**, 45.

Kendall, A. I., Day, A. A., and **Walker, A. W.** (2). **The metabolism of bovine tubercle bacilli.** *J. Infect. Dis.*, 1920, **26**, 77.

The authors have studied the chemical changes occurring in a 3 per cent. glycerol broth medium inoculated with two virulent cultures of tubercle bacilli of the *typus humanus.* An elaborate table indicates their results, from which it is apparent that the chemical changes in the two instances were very similar and consisted in the production of a feeble acid reaction with a decrease in ammonia, amino nitrogen, and total nitrogen in solution up to the point of maximum development of culture. After this, and apparently as a result of autolysis, a resolution of nitrogenous constituents becomes manifest and proceeds until a very considerable return to conditions in the original quantitative nitrogenous composition of the medium is obtained. The development of an acid reaction and the minimal evidence of deamination suggests that glycerol may be largely used for energy requirements and acts as a protein sparer.

Similar experiments on virulent and avirulent strains of bovine bacilli are described in the second paper, and show a small but definite increase in titrable alkalinity which is progressive. Generally speaking, the ammonia curves and curves of deamination are the reverse of those obtaining with virulent human tubercle bacilli. Increased ammonia production suggests increased action on the proteins, a view supported by the increase in amino acids. The whole action of the bovine bacilli is distinctly proteolytic and glycerol seems to be unable to act as a protein sparer. W. B.

Griffith, A. S. The bacteriological characteristics of tubercle bacilli from different kinds of human tuberculosis. *J. Path. & Bacteriol.*, 1920, **23**, 129.

In this paper the author gives his latest results in the classification of tubercle bacilli from human cases. Special reference is made to scrofulodermia.

Twelve cases of T. B. meningitis were examined. Ten of these were due to human type bacilli and two to bovine types. All of the patients were children and the two instances of bovine infection were the youngest.

Seventeen strains from pulmonary tubercle were examined, sixteen were human type, while one showed characters of human and bovine.

The cases of scrofulodermia numbered 60, and from these 52 cultures were obtained. Sixteen of these proved to be typical bovine strains, while four were atypical in that they showed diminished pathogenicity. The remaining 32 strains were human, and these also in some cases showed diminished pathogenicity.

In six cases of lupus half of the strains were human and half bovine; all were attenuated.

A table is appended which shows the results of the author's work to date upon 1,068 cases. It illustrates the relative unimportance of bovine type bacilli in human tuberculosis and the greater importance of these in the first years of life. P. F.

Moursund, W. H. Complement fixation in diagnosis of tuberculosis. *J. Infect. Dis.*, 1920, **26**, 85.

The author describes the results obtained with the sera of 186 patients. 103 being active cases and 51 inactive cases of phthisis. One was a case of tubercle of the epididymis and 31 were non-tuberculous. Petroff's antigen of dried tubercle bacilli extracted with methylic alcohol was used. The results, detailed in the paper, led the author to the conclusion that the complement fixation test for tuberculosis with the extract used is not specific and is of 'no value as a diagnostic or prognostic aid'.

W. B.

Gordon, J. E. The bacteriology of chronic empyema. *J. Infect. Dis.*, 1920, **26**, 29.

The author studied the bacteriology of 25 cases of empyema which had lasted from 2 to 17 months. With one exception a history of pneumonia, either primary or following measles or influenza, was given. In contradistinction to that of acute cases in which the leucocytosis is high, the chronic cases gave about 10,000 leucocytes per 3 mm. and a neutrophilia of 60–70 per cent. Enumeration of the bacteria in the exudates was carried out, the author recommending that the drainage tube should be removed and replaced by a sterile rubber tube of much smaller diameter and shorter. Through this a long looped needle is introduced and a quantity of the exudate is removed for microscopic examination. Cultures were made of every case at weekly periods during three months. Although one case gave a history of pneumococcic infection, pneumococcus was not found in any case. In the remaining 24 cases haemolytic streptococci were the primary invaders which caused the pleural suppuration. By the time that the cases had become chronic streptococci were found in only eleven. The principal microbes encountered were staphylococci, *B. proteus*, and especially one belonging to the Friedländer group and giving fermentation reactions like *B. mucosus* although it behaved as a distinct species. Diphtheroids were occasionally encountered, but never in large numbers. During the chronic empyema stage the sera of 20 of the cases were tested for agglutinating properties on a *Streptococcus pyogenes* isolated from one of them. All showed positive reactions, one of them giving a titre of 1:3,200. At the time of the test streptococci were absent from all the cases but one.

W. B.

Bull, C. G. and **Bartual, L. Pneumococcus cultures in whole fresh blood. I. The retardative effect of the blood of immune animals and the mechanism of the phenomenon.** *J. Exper. M.*, 1920, **31**, 233.

This paper concerns the alleged pneumococcidal action of the 'whole blood' of immune animals, and the author believes that this property is not so marked *in vitro* as has been claimed. Cultures of pneumococci in fresh whole blood of immune animals as compared with cultures in the blood of susceptible animals show a greatly prolonged latent period, the prolongation corresponding in a general way to the relative resistances of the animals to pneumococcic infections.

The blood of animals immunized actively and passively behaves like that of animals congenitally immune. Microscopic examination of cultures of pneumococci in immune blood shows chain formation, growth in clumps, and phagocytosis. Growth begins first in the serum, the clot being subsequently invaded. The author believes that the retardation of multiplication in immune serum depends on opsonization and phagocytosis by the polynuclear cells. Pneumococci multiply in defibrinated immune blood because few phagocytes are present. If the leucocytes are destroyed pneumococci grow in the most potent immune blood. W. B.

Embleton, Dennis. Sphenoidal empyema and epidemic cerebrospinal fever. *J. Roy. Army Med. Corps*, 1920, **34**, 236.

Details are given of 34 cases of cerebrospinal fever which ended fatally and were examined *post mortem*.

Empyema of the sphenoidal sinus was present in thirty-two of these cases.

Meningococci were cultured in ten of these cases. In ten more they were seen but not grown.

Forty-seven completely recovered cases were examined and no sphenoidal empyemata could be detected.

The author considers the appearance of a sphenoidal empyema to indicate a grave prognosis, and the course it runs to determine in all probability the ultimate result of the disease.

Various routes by which meningococci may reach the meninges are discussed and the author concludes that it is probable that they pass by way of the lymphatics from the sphenoidal sinus direct to the meninges, with or without naked-eye signs of inflammation.

Sphenoidal empyema was found in all cases where cerebrospinal fever was followed by hydrocephalus. G. T. W.

Klein, K. Ein neuer Diphtherienährboden. [**A new diphtheria culture medium.**] *Deutsche med. Wchnschr.*, 1920, **46**, 297.

On account of the difficulties of preparing Loeffler's serum for diphtheria examinations the author recommends an alkali albuminate prepared as follows: Nine parts of horse serum are mixed with 1 part of officinal sodium hydrate solution and kept at 37° C. for 2 days. The mixture is then neutralized with hydrochloric acid and one part is mixed with 4 of agar. Sterilization is carried out at 105° C. for ½ hour. Comparison with ordinary Loeffler's serum showed no difference in the frequence or character of the growths. The medium is recommended as being transparent, durable, and capable of being sterilized easily. W. B.

Durand, P. Non-absorption de l'antitoxine diphthérique par la muqueuse rectale. [**Diphtheria antitoxin is not absorbed from the rectal mucous membrane.**] *Compt. rend. Soc. de biol., Par.*, 1920, **83**, 403.

Attempts to observe whether the rectal injection of diphtheria antitoxin modifies the Schick reaction subsequently applied. In 14 children who received 20 to 30 c.c. of antitoxin per rectum no notable degree of immunity followed, as the Schick test was positive. This is in marked contrast to the effects following subcutaneous inoculation of smaller quantities of antitoxin. W. B.

Arloing, F. et **Richard, G.** Apparition de corpuscles métachromatiques chez les bacilles pseudodipthériques. Conditions de cultures favorisantes. [**Appearance of metachromatic granules in cultures of pseudo-diphtheria bacilli and the conditions which favour their development.**] *Compt. rend. Soc. de biol., Par.*, 1920, **83**, 401.

When cultures of pseudo-diphtheria bacilli, which show no metachromatic granules, are grown in media containing phosphorus compounds such as nucleoprotein or lecithin, typical metachromatic granules make their appearance. The appearance of granules is, however, not associated with an increase of virulence in such cultures. W. B.

Saphier, J. Zur Technik der Levaditi-Methode. [**The technique of the Levaditi method.**] *München. med. Wchnschr.*, 1920, **67**, 352.

The author recommends the following formula:

1. Fixation in 10 per cent. formalin (the longer the better).

2. Alcohol 90 per cent. for 24 hours.

3. Distilled water until the tissue sinks in it.

4. Two per cent. sol. of silver nitrate for 3 days at 37° C., the fluid being changed daily.

5. Wash for a short time in distilled water and place the tissue in ammonia pura liquida (concentrated) for 24 hours.

6. Reducing fluid consisting of pyrogallol 4·0, formalin (40 per cent.) 5·0, distilled water ad 100, for 24 hours. At first there is an abundant dense milky precipitate when the tissue is taken from the ammonia and placed in the reducer, necessitating several changes of the reducer during the first few minutes.

7. Alcohol fixation, toluol and paraffin embedding.

The author also recommends a quick process as follows:

1. Tissue is placed for 5 hours in 20 per cent. formalin [Formalin (40 per cent.), 10·03 aq. destil., 40·0.]
2. Five hours in 90 per cent. alcohol.
3. Ten to 20 min. in distilled water.
4. Twelve to 15 hours in 2 per cent. silver nitrate.
5. Ten to 15 min. in ammonia.

Processes 1 to 5 are carried out in the paraffin bath at 57° C.

6. Wash in distilled water and place in reducing bath at room temp. for 1–2 hours.

7. 70 per cent. alcohol and quick embedding. W. B.

Becker, E. Eine empfehlenswerte Methode für Spirochätenfärbungen. [**A method which can be recommended for staining spirochaetes.**] *Deutsche med. Wchnschr.*, 1920, **46**, 259.

This is a modification of Fontana's method, the tannin content being increased and the silver solution being replaced by Ziehl's fuchsin. The process is carried out as follows:

1. Fixation in Ruge's solution (glacial acetic acid 1·0, formalin 20, water 100), for 1 minute.

2. Tannin solution (10 per cent.) heated to the point of 'steaming' for ½ minute.

3. Stain in warm carbol fuchsin solution for ½–¾ minute. Wash, dry, and mount in neutral balsam. W. B.

Hoffmann, Erich. Ueber eine der Weilschen spirochäteähnliche Zahnspirochäte des Menschen (*Spir. trimerodonta*) und andere Mundspirochäten. [**A dental spirochaete (*Spir. trimerodonta*) similar to the spirochaete of Weil's disease.**] *Deutsche med. Wchnschr.*, 1920, **46**, 257.

In a study of the spirochaetae of the mouth, Hoffmann has noted in particular an organism possessing striking resemblance to *S. icterohaemorrhagica*, and proposes to call it *S. trimerodonta* on account of its three parts. What has hitherto been called *S. dentium* (denticola) can apparently be separated into three sub-groups: (1) *S. dentium* (Koch) proper, a fine, straight, spiral organism, which the author suggests might be called *S. orthodonta*. (2) A finer, peculiarly bent spirochaete slightly refractile and difficult to stain. This is *S. skoliodonta*. (3) Spirochaetes exactly like those found in Weil's disease and for which the name *S. trimerodonta* is suggested. The author suggests a morphological classification of buccal and dental spirochaetes as follows:

1. *S. buccalis* (Cohn).
    - a. *crassa* } coarser forms.
    - b. *tenuis* } coarser forms.
    - c. *inaequalis*? } coarser forms.
2. *S. media oris* (E. Hoffmann and v. Prowazek), of medium size.
3. *S. dentium* } fine forms.
4. *S. skoliodonta* } fine forms.
5. *S. trimerodonta* } fine forms.

W. B.

Levaditi, C. et Harvier, P. Recherches sur le virus de l'encéphalite léthargique. [**Researches on the virus of encephalitis lethargica.**] *Compt. rend. Soc. de biol., Par.*, 1920, **83**, 385.

This is a short note to the effect that the virus of encephalitis lethargica can be transmitted to rabbits by inoculation into the anterior chamber of the eye. The incubation period was seven days. Virus passed through rabbits is also pathogenic for guinea-pigs after an incubation period of 9–12 days, and from the nervous system of guinea-pigs the virus can again be transmitted to rabbits. The authors were unable to prevent a lethal infection when the virus was mixed with one or other of three sera from human beings convalescent from the disease. W. B.

Robertson, Muriel. Serological groupings of *Vibrion septique* and their relation to the production of toxin. *J. Path. & Bacteriol.*, 1920, **23**, 153.

Vibrion septique strains are divisible into at least three serological types by agglutination.

The toxin produced by the various strains was not dependent upon the source of the strain for its toxicity. An injection of from 0·1 c.c. to 1 c.c. intravenously into a rabbit usually killed in ten minutes.

Antitoxins made from single strains were found to neutralize the toxic effect of all other strains without reference to their serological type. Similarly each antitoxic serum will protect guinea-pigs from infection with all strains.

Thus the agglutination method as a means of subdivision of *vibrion septique* is ultraspecific and has no practical value. P. F.

Rous Peyton, Wilson, G. W., and **Oliver, J. Experiments on the production of specific antisera for infections of unknown cause. III. The effects of a serum precipitin on animals of the species furnishing the precipitinogen.** *J. Exper. M.*, 1920, **31**, 253.

Specific antisera for infections of which the exciting agent is unknown can be produced in some instances by the use of infected tissue itself as antigen. Such sera may, however, be toxic, the toxicity being due to antibodies produced by the tissue component of the antigen, such antibodies being injurious to animals of the species furnishing the antigen. Of antibodies the authors have specially studied, in the present communication, precipitins. They find that in serum of great precipitin titre, a highly toxic principle exists for animals of the species which furnish the antigen. Intravenously, such a serum produces shock, and even sudden death, while locally there may be acute inflammatory changes and profuse capillary haemorrhages. The complete removal of such antibodies as haemolysins and haemagglutinins lessens the toxicity only to a slight degree, while the further removal of precipitin has no detoxicating effect whatever. The practical bearing of this arises in cases where the serum of infected human beings might be employed as antigen to produce antisera in animals for passive immunization. Such antisera may be toxic, and the toxicity cannot be eliminated by exhausting the serum with red cells or other antigens to remove haemolysins, haemagglutinins, or precipitins. Nor can the toxicity be removed by desensitization as carried out in anaphylaxis. In the absence of an effective means of detoxicating the antisera, the authors consider that the body fluids of infected human beings should not be utilized for the production of therapeutic antisera. W. B.

Happ, W. M. Appearance of isoagglutinins in infants and children. *J. Exper. M.*, 1920, **31**, 313.

Although a great deal of work has been done on isoagglutinins in the blood of adult human beings, little is known of their occurrence at birth, and the author has sought to fill this lacuna. The isoagglutination reaction of 131 infants and children from birth to 10½ years, was examined by testing their sera and washed red corpuscles against the sera and corpuscles of each of the four adult Moss groups. The groups encountered in adults are rarely found in blood from the umbilical cord. At birth, and during the first month of life, isoagglutination is seldom met with, but the percentage of infants in which the isoagglutinin group is established, increases with age, so that after one year the group is usually established, and after two years is always present as in adults. The grouping is established in the corpuscles earlier than in the serum. In Ehrlich's language the corpuscles acquire agglutinophilic receptors before the serum acquires agglutinin. Therefore Group I of Moss is the first to appear, and Group IV the last.

The early grouping in the corpuscles, before the serum, is liable to change by the acquisition of new receptors. When the grouping has been established in both serum and corpuscles it does not change. The author finds that isoagglutinins are present in mother's milk, and the grouping is identical with that in mother's blood. He does not consider that the agglutinins are transmitted to the suckling through the milk. On account of the differences existing between agglutinin reactions in the blood of mother and child respectively, it is not safe to transfuse an infant from its mother without making the necessary preliminary tests.

W. B.

Oppenheimer, R. Ueber die bei Arbeitern chemischer Betriebe beobachteten Geschwülste des Harnapparates und deren Beziehungen zur allgemeinen Geschwulstpathogenese. [**On the tumours of the urinary apparatus in chemical workers, and their relation to general pathogenesis of tumours.**] *München. med. Wchnschr.*, 1920, **67**, 12.

Considerable interest was aroused some years ago when Rehn, in Frankfort, drew attention to the occurrence of vesical tumours in anilin workers, especially those connected with the manufacture of fuchsin. Between 1910 and 1919 there were 20 cases, 19 of which had the bladder affected, while the remaining case had a tumour in the posterior urethra. The substances incriminated in the blastomatous production were particularly benzidin, anilin, anilin dyes, anilin + naphthylamin, anilin + benzene + toluene. The tumours occurred not only in the workers with these substances, but also in workers in adjacent rooms.

From the date of exposure to the particular chemical until the development of symptoms 9½–28 years (average 18 years) elapsed. Even after cessation of all work with the dangerous chemical, tumours occurred in 10–17 years. Apparently there is a very long latent period before the tumour shows itself, and different types of growth may result from exposure to one and the same injurious chemical. It would also appear that the duration of the exposure and the intensity of the noxa play no definite part in determining the length of the latent period or the nature of the new growth. The prognosis of the cancerous growths is bad, of the papillomatous growths doubtful.

W. B.

Fairhall, L. T. and **Bates, P. M.** **The sterilization of oils by means of ultra-violet rays.** *J. Bact.*, 1920, **5**, 49.

The sterilization of oils in connexion with the preparation of lipovaccines has become a matter of some practical importance. The present authors have made a study of the disinfection by means of ultra-violet rays. Using a straight tube quartz mercury vapour lamp operating at 175 volts and 3·8 amperes, they find that olive, cotton-seed, and almond oils can be sterilized by a short exposure to ultra-violet rays. It was found that an emulsion of *B. subtilis* was almost completely sterilized within the first 60 seconds. Even spores of moulds like *Penicillium*, *Mucor*, and *Aspergillus* were killed. Lipolytic enzymes in oil were found to be sensitive to, and their action was inhibited by, exposure to the rays. Apart from a slight bleaching, the sterilized oils were unaltered physically or chemically. The depth of the oil layer through which the rays penetrated effectively was 4 mm.

W. B.

BIOCHEMISTRY

Mills, C. A. Activity of lung extracts as compared to the extracts of other tissues, in inducing coagulation of the blood. *J. Biol. Chem.*, 1920, **40**, 425.

Following up some work of Wherry and Ervin, the author has found that lung extracts are more active than extracts of other tissues in inducing intra- and extra-vascular clotting (the cause of sudden death produced by the injection of tissue extract). The order of activity for the different tissues is as follows: lung, kidney, heart, brain, spleen, thymus, testis, skin. The coagulative activity of lung and kidney tissue is probably of value to the animal in protecting it from haemorrhage in these vital parts.

R. A. P.

Van Slyke, L. L. and **Baker, J. C. Carbonic acid and carbonates in cows' milk. Conditions causing variation in the reaction of freshly drawn milk. A method for the preliminary detection of abnormal milk based upon the hydrogen- ion concentration. A method for the determination of the keeping quality of milk.** *J. Biol. Chem.*, 1920, **40**, 335–73.

In this series of papers, the authors have evolved a simple test for the preliminary detection of abnormal milk. They do not claim that it is in any way absolute, but hold that, when intelligently used, it may be of great value in the rapid separation of the good from the bad samples. In 300 samples of freshly drawn cows' milk they found that the limits of variation of the hydrogen-ion concentration were between P_H 6·50–7·20, being under 6·76 in 80 per cent. of the cases. P_H values over 6·80 were usually accompanied by large numbers of leucocytes in the sample, though the additional presence of acid-producing streptococci may induce a reverse effect. Blood or serum are usually present in this type of abnormal milk. By the use of the indicator brom-cresol purple under standard conditions, changes in the hydrogen-ion concentration can be detected. The colour of the indicator is lighter blue than normal in the presence of acids, acid salts, formaldehyde, or when the milk has been pasteurized; it is a darker blue than normal when the milk comes from diseased udders, or when it is watered or skimmed or has had an alkali or alkaline salt added to it. The brom-cresol test can be applied to the determination of the keeping quality of milk.

R. A. P.

Osborne, T. B. and **Wakeman, A. J. Extraction and concentration of the water-soluble vitamine from brewers' yeast.** *J. Biol. Chem.*, 1920, **40**, 383.

By fractional precipitation with alcohol, the authors have obtained a very active preparation of the water-soluble vitamine representing 7·5 per cent. of the nitrogen of the original yeast. They have obtained this upon a large scale and are studying it.

R. A. P.

Raizier, G. W., Kolmer, J. A., and **Gavron, J. L. Chemotherapeutic studies on organic compounds containing mercury and arsenic.** *J. Biol. Chem.*, 1920, **40**, 533.

The authors have prepared mercurial derivatives of various phenylarsenic acids with the hope of finding an organic compound containing both mercury and arsenic which is of superior value in the treatment of trypanosomiasis or of use as a general germicide. The results have been disappointing up to the present, but the authors hope that further research may lead to fruitful discovery. R. A. P.

McClendon, J. F., Cole, W. C. C., Engstrand, O., and **Middlekauff, J. E. Effect of malt and malt extracts on scurvy and the alkaline reserve of the blood.** *J. Biol. Chem.*, 1920, **40**, 244.

Extending the work of Fürst, Cohen, and Mendel, they have shown that sprouting cereal grains are rich in the antiscorbutic factor, especially after the acrospire projects half an inch beyond the end of the grain. The antiscorbutic factor is not destroyed by heating to 71° C., and may be extracted from sprouting barley by crushing in a roller close enough to rupture the acrospire cells. R. A. P.

Kendall, E. C. and **Osterberg, A. E. Chemical identification of thyroxin.** *J. Biol. Chem.*, 1920, **40**, 265.

This paper gives an account of the chemical and physical properties of the active principle of the thyroid gland, and should be consulted by those interested. The authors say that thyroxin exists in four distinct forms, keto form with imino carbonyl group, enol form in which the hydrogen migrates from the imino to the carbonyl forming the hydroxy group, an open ring form, and a tautomeric form of this. The molecular weight is 585, and the iodine content 85 per cent. The paper is of interest in connexion with Huxley's recent experiments on the acceleration of growth by the use of thyroxin. R. A. P.

Olmsted, W. H. Availability of carbohydrate in certain vegetables. *J. Biol. Chem.*, 1920, **41**, 45.

Spinach, cabbage, cauliflower, and lettuce are used in the diet of the diabetic during the determination of the sugar tolerance without a very accurate knowledge of their sugar content. They may also contain certain substances, such as organic acids, from which the organism might make sugar. These latter would not be shown as carbohydrate by the ordinary methods of reduction analysis. The carbohydrate in the above vegetables has been found by the author by two methods. By one the available sugar is found by hydrolysing with the starch ferment, taka-diastase, and subsequent sugar estimation, and by the other the substance is given to a dog poisoned with phloridzin. The author gives his results in tabular form. For the uncooked vegetables, there is not much difference from the results of Atwater and Bryant. On the whole there is a slightly larger amount of sugar shown by the physiological method. This may be within the limits of error, or may indicate a synthesis of sugar from non-carbohydrate material. There is, however, a very big decrease in the carbohydrate formed from the cooked vegetable. In cabbage, for instance, the available carbohydrate in the uncooked vegetable is 4·4 per cent., whereas in thrice cooked it is 0·4 per cent. R. A. P.

Tatam, A. L. Alkaline reserve capacity of whole blood and carbohydrate mobilization as affected by haemorrhage. *J. Biol. Chem.*, 1920, **41**, 59.

The paper deals with a further study of the reason why haemorrhage often produces hyperglycaemia. It is found that in rabbits, as the result of a properly graded haemorrhage, the CO_2 capacity of the blood seems to fall at the same time as the rise in blood-sugar appears. The recovery from both the change in alkaline reserve and the hyperglycaemia occurs within a few hours even in the fasting animal. The results of giving sodium bicarbonate seem to be a little conflicting. There is a slight balance in favour of thinking that haemorrhage is more readily produced after reducing the alkaline reserve by acid feeding, and less readily after feeding with alkalies. The author believes that his results support the view of Murlin and Underhill that the acid-base equilibrium in the blood (and consequently in the tissue cells) is an important controlling factor in sugar metabolism.
R. A. P.

Steenbock, H. and **Boutwell, P. W. Fat-soluble vitamine. 3. The comparative nutritive value of white and yellow maize.**

Steenbock, H. and **Cross, E. G. 4. The fat-soluble content of green plant tissues, together with some observations on their water-soluble vitamine content.**

Steenbock, H. and **Boutwell, P. W. 5. Thermostability of the fat-soluble vitamine in plant materials.** *J. Biol. Chem.*, 1920, **41**, 81, 149, 163.

In these three papers the authors have added to their studies on the fat-soluble vitamine. Again it is found that the fat-soluble vitamine and the yellow plant pigment are closely associated. Yellow maize gave normal growth with their rats, though not usually reproduction. White maize did not keep the rats alive longer than about three months. Leaves again are found to be the most rich in fat-soluble vitamine. Autoclaving for three hours at 15 pounds pressure did not destroy the fat-soluble vitamine in yellow maize, carrots, chard, sweet potatoes, or squash. R. A. P.

Stadie, W. C. A method for the determination of methaemoglobin in blood. *J. Biol. Chem.*, 1920, **41**, 237.

It is sometimes needed to know the content of a given blood in methaemoglobin. The usual method of finding this is complicated. The author has worked out a method for clinical work based upon the conversion of the methaemoglobin and haemoglobin in the blood to cyanhaemoglobin with potassium cyanide. The cyanhaemoglobin can be readily estimated with a colorimeter. By combining the value so obtained with a determination of the haemoglobin present in the blood by the oxygen method, the difference gives the methaemoglobin. R. A. P.

Zoller, H. F. Indole in biological media. Influence of hydrogen-ion concentration upon the volatility of indole. *J. Biol. Chem.*, 1920, **41**, 25 and 37.

The author has worked out the limitations of the nitroso-indole reaction of Baeyer in order to standardize the method of Nonnette and Demanche for the quantitative determination of indole. The author claims that it is simple and easy to apply. The indole is separated from the liquid to be examined by one direct distillation, dependent for its best condition upon the hydrogen-ion concentration. The vanillin test for indole is not regarded as satisfactory. R. A. P.

Stadie, W. C. and **Van Slyke, D. V. Studies of Acidosis. 15. Carbon dioxide capacity and content in arterial and venous blood plasma.** *J. Biol. Chem.*, 1920, **41**, 191.

The authors have had the opportunity of testing whether determinations of the CO_2 capacity of the venous blood in ordinary clinical work give a really reliable picture of the capacity of the arterial blood. They find that the CO_2 content of arterial and venous plasma run parallel, the latter being about one-tenth less. They conclude that it is quite justifiable to use a sample of venous plasma for determining the alkaline reserve if the blood is centrifuged and analysed without loss of CO_2. This is even true when the conditions of gaseous exchange in the lung become abnormal through pneumonia. R. A. P.

Myers, F. J. and **McClendon, J. F. Note on the hydrogen-ion concentration of the human duodenum.** *J. Biol. Chem.*, 1920, **41**, 187.

The reaction of the contents of the duodenum was found to vary round the neutral point. On the whole there was a greater tendency to an acid reaction than an alkaline one. The authors think that the best view to take of the mechanism of the opening of the pylorus is that acid influences the tone of the muscle. Whenever this is less than the tone of the stomach or duodenum the passage of fluid may occur. This will explain the occasional staining of the stomach contents with bile. R. A. P.

Kramer, B. Direct quantitative determination of potassium and sodium in small quantities of blood. *J. Biol. Chem.*, 1920, **41**, 263.

The author has found that the potassium content of normal human serum varies between 16 and 22 mg. per 100 c.c. The sodium content has been found in both normal children and adults to vary between 280 and 310 mg. per 100 c.c. of serum. The author intends to publish his experiments in detail later on. R. A. P.

Cohen, S. J. Studies on the secretion of gastric juice. *J. Biol Chem.*, 1920, **41**, 257.

The secretion of the acid juice of the stomach is always a biochemical mystery. There are two views as to the mechanism of this, one that the chlorides are secreted into the stomach at a constant rate and then intermittently converted to the acid. The other is that of Pawlow, who thinks that the acid is secreted as such into the stomach and then undergoes secondary neutralization. The author has done 175 chloride estimations on the gastric juice of various dogs in which high temperatures had been produced by means of injections of sodium nucleinate or of *B. prodigiosus*, or which had been treated otherwise. The free HCl in these cases varied from 0·0–0·48 per cent., while the total chlorides only varied from 0·39–0·54 per cent. The curves for the secretion of HCl and chlorides do not run parallel. The results of Pawlow are confirmed, that when there is a large secretion of gastric juice the acidity of the juice is higher, which on the Pawlow view is because there is less of the alkaline mucosa to neutralize the rapidly flowing juice. The author's experiments do not really decide between the two views ; he is waiting for a case of achylia, but has not yet been able to get one. R. A. P.

Sherman, H. C. (1) Protein requirement of maintenance in man and the nutritive efficiency of bread protein. (2) Phosphorus requirement of maintenance in man. *J. Biol. Chem.*, 1920, **41**, 97 and 173.

These two papers form a summary of the work of the author in collaboration with a great number of workers in his laboratory, and in the first paper on protein requirement he has also included in his results the experiments of other workers in the field so far as they can be shown to bear on the results. By taking an average of all the pertinent experiments, he finds that the protein requirement for maintenance calculated in terms of a man of 70 kilos is 45, 43, 41 grm. per day according as he includes in his average 109, 94, or 76 experiments. The chief cause of the large extremes of variation appearing in the literature viz., 21–65 grm., seems to lie in the differing length of the investigations and the extent to which the individual had accustomed himself to a low protein diet. The protein of wheat bread showed as high an efficiency in the maintenance metabolism of man as would be expected of the protein of a mixed diet, allowing for the use of a small amount of milk in the making of the bread. By a comparison of their experiments with the diet experiments of those who have worked upon rats, it is concluded that there is a very good general agreement between the protein requirement of man and the rat for maintenance, if the food is calculated in total calories of food consumed. *Maintenance* of course is a very different thing to *growth*, in which it has been shown so conclusively by Hopkins, and afterwards by Mendel and Osborne and McCollum that the individual constituent amino acids of the protein play such an important part. The results of tests carried out with cereals, viz. wheat, maize, and oats, showed that a diet in which about nine-tenths of the protein was derived from the cereal and the remainder from such a source as milk or apple, only 33–40 grm. of protein were needed to meet the protein requirement of adult nutrition. This is in disagreement with the results of Karl Thomas for wheat and maize, but agrees with those of Hindhede for wheat oread.

So it appears from recent work that, even when the protein of the food is largely derived from the bread or other grain products, a standard allowance of 1 grm. per kilo of body weight should allow a margin of safety of 50–100 per cent. as far as the requirements of adult *maintenance* are concerned. This of course does not touch the importance of the supply of the vitamine constitutents of the diet by small quantities of milk, &c.

The second paper is a summary of the maintenance requirement for the adult of phosphorus, from data accumulated during the past 15 years in Columbia University. The average of the 95 experiments shows a need of 0·88 grm. of phosphorus per day per 70 kilos of body weight, the experiments varying from 0·52–1·20 grm. During recent years it has been the tendency to assume that the form in which the phosphorus was taken does not matter. It may be that some of the variations of these experiments are the expression of the fact that the form in which phosphorus is taken cannot be neglected. In a detailed study of the food supplies of 224 families from the United States only 8 showed less than 0·88 grm. of phosphorus per day. Now that the phosphorus requirement of maintenance is known it will be possible to determine the increase or otherwise needed for growth, pregnancy, and lactation. R. A. P.

Bordet, J. Serum origin of an aphylatoxin and anti-anaphylaxis. *Bull. Acad. roy. de méd. de Belg.*, 1919, **29**, 635. (*Chem. Abstr.*, 1920, **14**, 567.)

As Bordet has previously shown, serum incubated with one-fifth its volume of 0·25 per cent. agar solution causes anaphylactic shock when injected into guinea-pigs. It is now shown that anaphylatoxin production takes place *in vivo* as well, since 1 c.c. of a 0·25 per cent. solution of agar causes typical fatal shock in a 400–600 grm. guinea-pig in 6–8 minutes. A preliminary dose of 0·5 c.c. protects against shock. The serum of an animal so treated is incapable of forming anaphylatoxin when incubated with agar solution or even with red corpuscles containing a specific antibody. This may be explained by the assumption in the sera of treated animals of a substance antagonistic to anaphylatoxin. In these experiments with agar the anti-anaphylactic state is produced under conditions excluding all participation of specific immune bodies and is reflected by the properties of the serum. C. G. L. W.

Bayliss, W. M. Capillary circulation. *Sci. Progress*, 1919, **14**, 272. (*Chem. Abstr.*, 1920, **14**, 561.)

A discussion, with bibliography of the chemical and physiological factors governing the circulation of blood in the capillaries.
C. G. L. W.

Dox, A. W. Experiments with soy bean meal as a substitute in the army ration. *Proc. Iowa Acad. Sci.*, 1918, **25**, 517. (*Chem. Abstr.*, 1920, **14**, 557.)

A mixture of 80 per cent. wheat flour and 20 per cent, soy bean flour yields an excellent bread of good flavour. Ten per cent. of soy bean flour is probably the optimum amount. It has a high protein content with a digestibility coefficient of 90 per cent. C. G. L. W.

Gregersen, J. P. Studies on occult blood. *Arch. f. Verdauungskr.*, 1919, **25**, 169. (*Chem. Abstr.*, 1920, **14**, 551.)

A comparison of several methods of determining occult blood was made. Gregersen suggests the following test, which has the advantage of being stable and is not too sensitive.

Powders are made up containing 0·025 grm. benzidine and 0·10 barium oxide. A 50 per cent. solution of acetic acid is also required. When a test is made, one of the powders is added to 5·0 c.c. of the acetic acid reagent, and 2–4 drops of the combined reagent are put on a smear of the material to be tested on a glass slide. The development of a blue-green colour within a minute is taken as a positive result. After this time the results are worthless. The reagent must not be used after it has stood 30 minutes.
C. G. L. W.

Baskerville, C. Chlorine and influenza. *J. Med. and Eng. Chem.*, 1920, **12**, 293.

Reports received from 25 producers of chlorine seem to point to this gas having a pronounced prophylactic effect. It seems to minimize the severity of the disease. One plant gave a decided opinion against the usefulness of the gas. In another, during the first epidemic all the workers were practically exempt, but in a second epidemic nearly all the workers suffered from influenza. The author is of the opinion that small concentrations of chlorine may be helpful. C. G. L. W.

Bordas. Use of hydrogenated oils as foods. *Ann. falsifications*, 1919, **12**, 225. (*Chem. Abstr.*, 1920, **14**, 580.)

At the request of the French Minister of the Interior, Bordas has investigated the suitability of hydrogenated oils for edible purposes and reports that there is no reason why fats produced by hydrogenating oils should not be used as food. The quantity of nickel in the products is extremely small, and is not harmful. Relatively large doses of nickel salts (up to 0·5 grm. of nickel during 52 days) are without injurious effect.
C. G. L. W.

Glibert. Occupational cancer. *Bull. Acad. roy. de méd. de Belg.*, 1919, **29**, 627. (*Chem. Abstr.*, 1920, **14**, 574.)

Largely a discussion of recent English experiences. This brings out that only the tars and pitches from certain coals are particularly dangerous, these being mainly of the bituminous type. Glibert thinks that possibly the harmful arsenic compounds are formed during the transformation of the coal into pitch and tar. C. G. L. W.

Macht, D. I. On the anthelmintic action of benzyl alcohol and benzyl esters. *J. Pharmacol. & Exper. Therap.*, 1919, **14**, 323.

Benzyl alcohol is toxic for earth-worms, and after a long interval for the round worms of the pig. A few clinical tests were made, but a more extended study is required. H. E. R.

Heinekamp, W. J. R. I. The action of adrenalin on the heart. II. The modification of the action of adrenalin by morphin. *J. Pharmacol. & Exper. Therap.*, 1919, **14**, 327.

Adrenalin has a central action synergic with morphin. Morphin sensitizes the vagus centre. Increased blood-pressure plays but little part in producing the inhibition of the heart. H. E. R.

Sollmann, T. Comparative toxicity of local anaesthetics and of antipyretics for earth-worms. *J. Pharmacol. & Exper. Therap.*, 1919, **14**, 319.

As a test for the clinical toxicity of antipyretics earth-worms are not suitable: the lethal action on earth-worms is a different mechanism from that of antipyretics in the human subject. H. E. R.

Dudley, H. W. Some observations on the active principles of the pituitary gland. *J. Pharmacol. & Exper. Therap.*, 1919, **14**, 295.

The nature of the active substances obtained from the posterior lobe of the pituitary gland is the subject of much investigation. The author has isolated crystalline residues with high physiological activity. The uterine stimulant is not histamin because there are marked differences in behaviour to certain reagents. During the process of preparation there is a partial separation of the pressor substance from the uterine stimulant.

H. E. R.

Mills, C. A. Cocaine intoxication in the rabbit. *J. Pharmacol. & Exper. Therap.*, 1919, **14**, 355.

There were no cumulative effects. The sensitizing effect on the iris lasts for twenty-five hours.

H. E. R.

Stewart, G. N. and **Rogoff, J. M. The action of drugs on the output of epinephrin from the adrenals. V. Curare.** *J. Pharmacol. & Exper. Therap.*, 1919, **14**, 343.

Curare in doses sufficient to paralyse muscles decreases the output of adrenalin: Curare should not be used in experiments on the output of adrenalin.

H. E. R.

Bisgaard, A. and **Nörvig, J.** Fortsatte Undersögelser over Neutralitetsregulation ved genuin Epilepsi. [**The ammonia content of the blood and the neutrality regulation in epilepsy.**] *Hosp.-Tid.*, 1920, **63**, 49–62.

The writers, whose first report appeared in *Hospitalstidende* No. 29, 1918, give in the present publication a preliminary account of their work up to date. Their material consisted of 16 cases of epilepsy and a few normal controls, and the number of examinations made was about 2,000. In their estimation of the ammonia content of the blood, they adopted the technique described by Henriques and Christiansen (*Biochem. Ztschr.*, 1916, **78**, 165) with minor modifications. The normal being taken as 0·3 to 0·4 mg. NH_3–N per 100 c.cm. of blood (Henriques and others), marked deviations from the normal, ranging from 0 to 1·42 mg. N, were found among the epileptics examined. The higher figures were obtained with much regularity shortly before an attack; thus there would be 0·67 mg. N three hours before an attack, and 14·2 N an hour before. During the 'psychic equivalent' of an epileptic attack, the figure would be 0·83 mg. N. The lower figures were never found before an attack; directly after an attack 0·29 mg. N were found. The writers conclude this section of their paper with the claim that, by their demonstration of the increased ammonia content of the blood in epilepsy, evidence of a well-defined endogenous poison has for the first time been provided in association with mental disease.

The urea content of the blood in epilepsy showed little deviation from the normal; it was slightly subnormal when the ammonia content was subnormal. The excretion of ammonia in the urine was also investigated, and compared with the ammonia content of the blood. The results were checked by a comparison with Hasselbalch's findings (*Biochem. Ztschr.*, 1916, **74**, 18). The writers then compare the metabolism (calcium metabolism, as shown by the condition of the enamel, albumin-metabolism, and NH_3

metabolism) characteristic of the three conditions, hypoparathyroidism in animals, tetany, and epilepsy, and they find striking uniformity in all. The most important difference is the absence in epilepsy of spasmophilic reactions which are common to hypoparathyroidism and tetany. The writers conclude that their investigations strengthen the view that genuine epilepsy is associated with hypo-function of the parathyroids. The recognition of a parathyroid epilepsy as a disease *sui generis* may also be followed by a subdivision of this disease according as the ordinary cases differ.

C. L.

Lauritzen, M. Forholdet mellem Kreatinuri og Acidose ved Sukkersygen. [**The relation between creatinuria and acidosis in diabetes.**] *Ugesk. f. Læger.*, 1919, **81**, 1595–1605.

After a résumé of the literature of this subject and a description of the technique he has adopted, Lauritzen gives details of several cases of diabetes illustrated with charts, in which he analysed the daily excretion of nitrogen, creatin, and ammonia. The first case showed that the excretion of creatin followed a curve parallel with that of the excretion of ammonia. Only during two 'hunger days' did these two curves fail to run parallel. This parallelism of the creatinuria and ammonia excretion was also observed in several other cases. In one case the acetonuria and diaceturia were greatest when the creatinuria was at its highest. Lauritzen suggests that the curves of creatinuria and ammonia excretion ran parallel because the diabetic diet affected the acidosis and creatinuria in the same way. When, in slight cases of diabetes, creatinuria appears before acetonuria, this, he suggests, shows that restriction of carbohydrates in the diet leads to creatinuria more readily than to acetonuria. He believes that there is insufficient evidence for assuming that acidosis *per se* leads to creatinuria in diabetes. It is more probable that faulty carbohydrate metabolism is the common cause of both these conditions. He dismisses as untenable the hypothesis that the creatinuria of diabetes is due to incomplete conversion of creatin to creatinin, with consequent excretion of creatin in the urine.

Probably the demonstration of creatinuria before the development of acetonuria will prove of little value in connexion with the early diagnosis of a pre-comatose state, for its onset is indicated by symptoms easier to gauge than creatinuria. But it may be of benefit to the diabetic that creatinuria is combated, for if it is protracted it may contribute to weakness of the muscular system. And, as these investigations show, creatinuria can be controlled by the same dietetic treatment that reduces acidosis. The degree of creatinuria is of prognostic significance: if it is considerable and continuous, it is of bad omen.

C. L.

RADIOLOGY AND ELECTROLOGY

Radio-diagnosis

Cotton, A. and **McCleary, S. Myxoma of bone with report of a case of myxochondro-sarcoma of the femur.** *Am. J. Roentgenol.*, 1919, **6**, 594.

A sufficient description of the case with radiographs at various periods is given, together with indications for treatment. The most interesting and newest point lies in the evidence afforded by the early radiographs that the tumour was of medullary or endosteal origin: there was no evidence whatever of periosteal change until immediately before amputation, but at that time there was thinning of the bone together with periosteal new bone formation along the inner surface of the shaft. These cases of what appears to be at first a simple myxoma that ultimately develops along sarcomatous lines—frequently after repeated operation—are little understood. It is generally considered that they originate in the periosteum or in the connective tissue of the attached muscle; but there are difficulties in the way of accepting this as an explanation, not the least of which is the fact that the tumours in question seem to arise as a rule about the epiphysial line. An endosteal origin seems more reasonable, and early radiological examination of future cases should settle the point. W. S. L.-B.

Moore, A. B. A synoptical examination of the seats of malignant metastasis in 65 cases where the bones were affected. *Am. J. Roentgenol.*, 1919, **6**, 589.

Two types of secondary bone metastases occur, viz. the osteoclastic and the osteoplastic. The osteoclastic form is characterized by marked lacunar absorption and destruction of bone, causing an extreme porosis of the osseous tissue. The osteoplastic form is characterized also by lacunar absorption, but there is thickening of the bone due to collection of malignant cells and to a secondary calcification around the malignant process. Both varieties often occur side by side. The radiological appearances differ accordingly, but M. agrees with Pfahler that the osteoplastic form is commonest in carcinoma of the prostate, while the osteoclastic is commonest in mammary carcinoma. The actual observations were made at the Mayo Clinic, and the commonest primary sites were breast and prostate, while the commonest seats of bony metastasis were spine, pelvis, femur, ribs, and humerus in descending order of frequency. It is impossible to criticize the figures given without much more information, but the order of frequency given above is somewhat surprising. It is certain, however, that malignant disease shows many and great variations in incidence in different countries in respect of primary sites, and the same may be true also in respect of sites of metastases. W. S. L.-B.

Déjerine, Mme and **Ceillier, M. A.** Para-arthropathies du genou chez les paraplégiques. [**Para-arthropathies of the knee in paraplegics.**] *Rev. neurol.*, 1918, Nos. 11–12, 348. (*J. de radiol. et d'électrol.*, 1919, **3**, 374.)

This communication deals with osteophytes near the articular surfaces of the knee in paraplegics suffering from traumatic lesion of the spinal cord.

By means of radiography, it is seen that the bony outgrowths are entirely extra-articular and appear to start at the internal condyle. The osteophytes, from three to six in number, have a shell-like or shield-like appearance and fit closely to the condyle, but without fusing with it. They are often bilateral. By X-ray examination, one sees that the morphological integrity of the skeleton is intact, the bony new growths being only in relation to it. This serves to differentiate this condition from chronic rheumatoid arthritis, where, according to Barjon, there are lesions of the skeleton and disappearance of the articular interspace.

There is, however, much similarity between the para-arthropathies of paraplegics and the tabetic and syringomyelitis arthropathies. By early examination, one could describe a 'pre-arthropathic stage of tabes'. At this stage the lesions are undoubtedly, in many of the cases, chiefly or entirely extra-articular. R. W. A. S.

Chaoul. Die radiologische Untersuchung des Duodenums unter Verwendung einer neuen Lagerungsvorrichtung für Aufnahme und Durchleuchtung. [**Radiological examination of the duodenum by means of a new method of exposure and screening.**] *München. med. Wchnschr.*, 1918, **65**. (*Zentralbl. f. Chir.*, 1919, **46**, 170.)

The method depends upon blockage of the lower transverse portion of the duodenum by compression of an oblong pad between the spinal column and the compression-tube. The patient has previously been given a barium-meal and is examined in the right latero-ventral position. As a result of obstructing the indicated portion of duodenum between the vertebral column and the abdominal wall, the gastro-intestinal tract from fundus of stomach to descending portion of duodenum becomes filled. Hence, from the presence or absence of certain characteristic departures from the normal X-ray appearances (defects at fundus or pylorus, hour-glass formation, diverticula, &c.), diagnosis with reference to ulcer is certain. In order that it might be possible to make a screen examination before the negative is taken, the author has constructed an apparatus which permits the patient to be moved from the prone position through any angle until he comes to lie directly on his side. He can be secured in the desired position and screened without the necessity of darkening the X-ray room, while the rays can be centred. Compression of the patient can be carried out and the plate can be exposed immediately after each radioscopic examination without any displacement of the screen or tube, by using a bonnet fluoroscope in place of the ordinary fluorescent screen. S. U. L.-B.

Béclère, H. et **Duval, P.** Radiographie positive de sept calculs du cholédoque. [**Positive radiography of seven calculi of the bile-duct.**] *Bull. et mém. Soc. de chir. de Par.*, 1919, **45**, 1304. (*Arch. d'électric. méd.*, 1919, **27**, 317.)

The authors present an exceptional case of a radiograph showing clearly seven calculi in the principal bile-duct in a woman of 55, who was being treated for biliary lithiasis of long standing, which for several months had been complicated by an intermittent retention-jaundice and fever. The radiograph taken by M. Béclère showed: (1) a group of nine calculi under the external extremity of the 12th rib, situated in the gall-bladder; (2) a second group of seven superposed calculi reaching from the first lumbar transverse process to the third, and following a curved line concave inwards; these were localized in the bile-duct. Operation confirmed the diagnosis. Radiographic examination of the calculi showed that they were formed of several opaque nuclei, of which one was generally central and was enclosed in a mass more permeable by the rays. The opaque nucleus was composed of bile pigments associated with mineral elements, among which lime predominated (20 per cent.). The radiological method was as follows: The patient was fasting, was purged the night before the examination, and had an injection two hours before the negative was made. The radiograph was taken in the ventral position, preceded by a radioscopic orientation on the gall-bladder and on the dorsal region, in order to mark the point of emergence of the normal ray. A localizing compressor was used with four to five Benoist rays and the patient held her breath during an exposure of six seconds. A Coolidge tube and an intensity of 13 milliamp. were used. The first positive case of radiography of calculi in the bile-duct, and the only one known to the authors, was that of Arcelin.[1] From American literature, although one cannot find precise information of differential diagnosis of the seat of the biliary calculi in the bladder or in the bile-duct, it seems that the radiologists have tried to ascertain their position in the bile-ducts. S. U. L.-B.

Engels. Über das Blutergelenk und sein Röntgenbild. [**Effusion of blood into joints and its radiographic appearance.**] *Fortschr. a. d. Geb. d. Röntgenstrahlen,* **25**, Heft 3. (*Zentralbl. f. Chir.*, 1919, **46**, 340.)

It is easily possible to confuse blood in the knee-joint with tubercular knee-joint; the skin is just as pale and cool, but the tubercular joint is more stationary. Later stages of the condition may be compared with the diseased joint in tabes. The author observed the case of a compositor of 25. He was a recognized bleeder, and this diagnosis was confirmed by blood-investigation. The disease of his knee-joint was of ten years' standing. The right knee was much thicker than the left. The muscles had absolutely disappeared. The joint was painful only after pressure, not to a blow. There was fluctuation in the degree of swelling. The radiograph showed great changes in the surfaces of the joint; these were flattened towards the side and showed spurs and bony projections. The cavity of the joint was small, particularly on the lateral side. The ends of the bones showed the presence of many irregular lighter spots as large as peas, situated towards the flat parts and particularly on the inner and outer sides: the outlines of many of these were ill-defined and cloudy. Shadows of calcification nearly as dense as bone shadows reached from the intercondyloid region to the tibia. At the back of the joint the soft parts (convex outwards, i. e. the capsule) appeared much thickened and calcified. The regions of thinning were almost everywhere surrounded by dense bone. Ill-defined, almost crateriform appearances were sometimes indicated and appeared to open into the joint. The fossa intercondyloides had broadened to the shape of a bowl. The infra-patellar ligament had curved forwards, and there were osteophytes on the patella. The inner condyle protruded far forward. A control-plate of the other knee showed that there was here no atrophy, that the appearances were less sharp, the ridges were less distinct; the knee as a whole gave a denser, more compact impression. The left knee also showed changes, but they were much slighter. The author considers that the X-ray appearances of this case are typical of the disease. S. U. L.-B.

Case, J. T. De la valeur de l'examen radiologique dans la lithiase biliaire. [**The value of radiological examination in cholelithiasis.**] *J. de méd. de Par.*, 1919, Oct. (*Arch. d'électric. méd.*, 1919, **27**, 319.)

Calculi containing less than 0·30 per. cent. of CaO are invisible on the radiographic plate; between 0·30 per cent. and 0·425 per cent. they can be seen in the best-taken radiographs with the help of good oblique lighting; containing over 0·425 per cent. of CaO they are easily seen. It is easily understood from the small proportion of lime necessary for detection that 45–50 per cent. of calculi cases can be demonstrated by radiography. The author bases his statements on several statistics of which two were personally made: (1) in 19 patients out of 1,000 examined for digestive affections, the calculi were visible forty-eight times on the plate: (2) in a series of 300 laparotomies in which the gall-bladder was examined as a routine, there were 41 cases of lithiasis, and of these 20 had been reported as positive on pre-operative examination. S. U. L.-B.

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[1] *Lyon méd.*, 1913, p. 112

Lorenz. Die röntgenographische Darstellung des subskapularen Raumes und des Schenkelhalses im Querschnitt. [**The radiographic appearance of the subscapular fossa and of the neck of the femur in cross-section.**] *Fortschr. a. d. Geb. d. Röntgenstrahlen,* **25**, Hft. 4. (*Zentralbl. f. Chir.,* 1919, **46**, 230.)

The radiograph of the subscapular fossa is taken with the subject in an oblique (lateral) position, with the head of the humerus immediately over the plate and the hand of the injured side placed high on the shoulder of the sound side. In severe injury of the soft part and of the head of the humerus itself this is not possible on account of the pressure. The neck of the femur in cross-section is obtained if the sound femur be flexed at an angle of 90° approximately. The plate is placed on the outside of the affected leg, and the orifice of the tube is brought under the upper part of the sound thigh and up to the inner side of the thigh of which the radiograph is to be taken. S. U. L.-B.

Radiotherapy

Mottram, J. C. and **Clarke, T. R. The leucocyte blood-content of those handling radium for therapeutic purposes.** *Proc. Roy. Soc. Med.* (*Electrotherapeutic Sect.*), 1920, **13**, 25.

The authors examined the bloods of various groups occupied at the Radium Institute, London, dividing them into (A) laboratory workers who prepare and measure applicators containing emanation and radium: (B) clinical workers who attach various screens to the radium applicators and subsequently apply them to patients. The remaining workers receive less exposure down to the servants of the institution, who are only subject to very small quantities of the gamma radiation which pervades the whole building. Compared with normal individuals, the polynuclear and lympholytic blood-counts of the radium workers are decidedly lower, and the most marked examples were found in the A and B classes. Of twenty individuals examined, the polynuclear count in eleven was lower than the lowest normal, and the lymphocyte count in three was lower than the lowest normal. No evidence of a leucocytosis was found in any individual, and the leucopenia came on after a very few weeks' exposure in an individual of the A or B class. Thus a class A individual showed a fall from 7,283 to 3,077 polynuclears and from 4,544 to 1,612 lymphocytes after a month; the corresponding figures for a class B worker were 4,448 to 2,398 and

1,824 to 1,690 in two weeks. A two months' holiday given to a worker with 522 polynuclears and 885 lymphocytes led to a rise to 1,909 and 2,158 respectively, and these figures, after 25 days' further work in the Institute, had fallen to 1,063 and 857 respectively. No association between the leucopenia and any condition of ill-health has been definitely recorded. An attempt was made to estimate the daily amount of irradiation which workers of class B receive. A photographic method was used and it was concluded that the entire front surface of the worker received about $\frac{1}{900}$ Rad. daily per sq. cm. Translated into terms of the dose of radiation administered in a typical radium treatment for cancer of the breast, such a class B worker would receive daily about 1·4 per cent. of the total radiation received by a patient during a course of treatment for carcinoma. Hence, every ten weeks such a worker receives the same quantity of radiation as a patient undergoing treatment for cancer of the breast. But whereas in the case of the patient the treatment is concentrated over a small area, in the case of the class B worker the radiation is spread over the whole body surface.

Similar, but less marked blood changes have been described in X-ray workers, and a leucopenia has been produced experimentally in animals with X-rays. In the subsequent discussion it was pointed out that in animals a leucocytosis was only observed with discontinuous exposure to X-rays: here the exposure to radiation was daily, and therefore leucocytosis was hardly to be expected. The amount of radium bromide distributed in applicators at the Institute is about 2·5 grm.

W. S. L.-B.

Nordentöft, S. 50 röntgenbehandelte Fälle von Morbus Basedowi. [**50 cases of Graves's disease treated by X-rays.**] *Ugesk. f. Laeger.*, 1918, **80**, 1331–71. (*Zentralbl. f. Chir.*, 1919, **46**, 230.)

Reports of 50 cases are given. The result was very good and often very striking after one seance. The 50 cases received in all 99 irradiations on the neck, and 84 over the region of the thymus. Operations were not performed without previous examination of the X-ray treatment.

S. U. L.-B.

Stepp, W. and **Czermak, R.** Über die bewusste Erzeugung und Verwertung der Secundärstrahlen bei der Röntgentherapie. [**The intentional production and use of secondary radiation in X-ray treatment.**] *München. med. Wchnschr.*, 1918, **65**. (*Zentralbl. f. Chir.*, 1919, **46**, 339.)

In order to intensify the irradiation of diseased parts by the production of specific secondary rays, the authors introduced chemical substances into hollow viscera; e.g. into the bladder, collargol solution (1 per cent.), iodoform-glycerine into joints, silver salts into the superficial layers of the skin and also into enlarged thyroid glands, or potassium iodide in internal tumours. They then administered 40 X over the same skin area during a period of 3–4 weeks. In nearly every case there was considerable improvement, such as would not have been obtained by deep irradiation.

S. U. L.-B.

Loose. Der Sieg der Röntgenstrahlen über den Brustkrebs. [**The triumph of X-rays over cancer of the breast.**] *München. med. Wchnschr.*, 1918, **65**. (*Centralbl. f. Chir.*. 1918, **45**, 915.)

L. states that he always obtained better and more certain results from very early X-ray treatment in cancer of the breast following on early operation. He also refers to the results in slighter and in more severe recurrences and metastases, and in cases which had previously neither been operated upon nor X-rayed. While improvement from X-ray treatment could be found in cases with slight recurrence and in those of lymphatic metastases, the more severe cases could not be cured. He asserts that by X-ray treatment in all cases in which no lymphatic metastases are clinically recognizable, their development can be prevented, and that glands already infiltrated have been caused to disappear completely. Finally, he refers to two unquestionable cases of cancer in the second breast after the first breast had been removed; two séances of X-rays caused the cancer on this side to disappear. The patients were still free from cancer a year later. On general grounds he argues against operation for cancer of the breast.

W. S. L.-B.

Electro-diagnosis.

Pieron, H. Du rôle joué par les pertes physiologiques d'énergie dans la relation qui unit le temps de latence sensorielle à l'intensité de l'excitation. [**Effect of physiological loss of energy on the relation which obtains between the sensory latent period and the intensity of the excitation.**] *Compt. rend. Acad. d. sc.*, 1919, June. (*J. de radiol. et d'électrol.*, 1919, **3**, 478.)

The latent period of sensory reactions decreases as the intensity of the excitation increases. If a be taken as the weakest intensity of excitation necessary for a reaction (threshold intensity), and if the period of latency corresponding to this threshold intensity be taken as unity, the period of latency y corresponding to any intensity of excitation x, greater than threshold intensity a, is given by the formula $y = \frac{a}{x^n}$, in which n is a constant that may be represented as a coefficient of the rapidity of the decrease. The author adds to this formula that of Weiss on the quantity of electricity q or it necessary to produce minimal excitation. When the duration t of excitation is progressively increased $it = a + bt$ in which a represents the threshold quantity of electricity necessary to provoke a response when the duration of the stimulus is infinitely small, and b the factor necessary to counterbalance the increasing current with the duration of excitation. The explanation is as follows: Weiss's formula enables one to define the duration of excitation for a given intensity; a current of intensity i will not provoke a response unless its duration t is sufficient to make the acting quantity it equal to the minimum term $a + bt$.

He assimilates the minimal duration in which an electric excitation of determined intensity must act, to the duration of the latent period mentioned. There is evidently a point open to criticism in this assimilation, and the author, while realizing this, ignores it, and continues his reasoning thus: t, Weiss's duration of excitation, is given by the equation $t = \frac{a}{i - b}$.

In other words, this duration is equal to the quotient of the threshold quantity for infinitely short waves a, divided by the difference $i-b$ between the proposed intensity i and the intensity b of the continuous current of infinite duration giving the threshold excitation.

By using y as above, for the duration (assimulated to the period of latency), and x for the proposed intensity, the formula becomes $y = \frac{a}{x-b}$. The author studied the decrease in the latent period of sensation corresponding to electric excitation of the skin in the frog, and finally tabulated his results according to the two following equations:

$$y = \frac{a}{xc} + k \text{ and } y = \frac{a}{x-b} + k.$$

With rapid waves, b practically disappears from the formula—that is, the physiological leakage phenomena are negligible. In spite of the fact that the interpretation of these studies contains matter for discussion, too much attention cannot be paid to researches which tend to establish precise connexion between the magnitude and duration of an external stimulus on the one hand, and the response, sensory or motor, on the other. It seems that Weiss's law more and more assumes a general character which brings it into a series of phenomena in the domain of irritability.

S. U. L.-B.

MEDICAL SCIENCE

ABSTRACTS & REVIEWS

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REVIEWS

DIABETES

Aetiology. (1) *Heredity.* Among 37 cases of diabetes studied in the diabetic service at U. S. Army General Hospital No. 9, Lakewood, New Jersey, Allen and Mitchell found six cases with a history of diabetes in the relatives. (2) *Syphilis* was demonstrated in four cases. (3) *Nervous hypothesis.* The writers emphasize the fact that the rarity of glycosuria after injuries is the striking lesson of the war. Only one of the 37 cases was an instance of this kind, the onset of glycosuria apparently dating from a tremendous shock. This case proved to be one of renal glycosuria. While nervous lesions are not excluded as affecting diabetes when the disease or predisposition is present, the experience of the war has clearly shown that the epidemic of diabetes, which was to be expected on the nervous hypothesis, did not occur.

In an article on **diabetes and syphilis** Ravogli reviews the literature and reports several personal cases to prove that the association of diabetes and syphilis is not a mere coincidence, though he does not of course dispute that diabetes as the result of pancreatic disturbance can be produced by many different causes. Diabetes may be the result of a syphilitic attack on the islands of Langerhans impairing the formation of the beta cells which produce the hormone to oxidize the sugar in the system. According to Mitchell, who reports an illustrative case in a man aged 43, although diabetes is relatively seldom due to syphilis, search for this cause, whether inherited or acquired, should be carefully made by all possible means. Probably as a rule diabetes, especially in an advanced stage, is not perceptibly affected by antisyphilitic treatment, as syphilis has presumably produced fibrous changes in the pancreas similar to those in the liver. The object of such treatment is merely to check further advance of the infectious process.

Carnot and Harvier point out that though the association of syphilis of the nervous system with diabetes has been reported by several observers, records of diabetes due to syphilitic pancreatitis are extremely rare and are not conclusive. They relate a case in a woman aged 53 who presented syphilitic nervous lesions (incomplete tabes and sacral anterior poliomyelitis) together with symptoms of diabetes and abundant glycosuria (300 gm. of sugar in 24 hours). At the autopsy sclero-gummatous pancreatitis was found combined with syphilitic cirrhosis of the liver. Apart from cases in which anatomical confirmation was lacking, the writers have found only four cases in the literature of diabetes due to syphilitic pancreatitis. A detailed report of these cases will be found in the Paris thesis written at their suggestion by Beguier, who considers that syphilis of the pancreas is more frequent than is generally supposed and that more cases of the kind would be reported if the diagnosis of the lesion could be made otherwise than by post-mortem examination. Syphilitic sclerosis of the pancreas is almost always associated with a rapid form of diabetes because this lesion represents such an extensive anatomical change.

Diabetes and exophthalmic goitre. The association of diabetes with exophthalmic goitre was described by Dumontpallier in 1867 and has since been noted by several observers. An editorial writer in a recent number of the *Medical Record* regards the association as rather uncommon, although some authorities, especially Apert, maintain the contrary opinion. Out of a total of 32 cases of exophthalmic goitre Griffiths found glycosuria in only two, and Naunyn states that he has never discovered it in the numerous cases of Graves's disease treated at the Strasburg Medical Clinique. Among 90 cases of exophthalmic goitre Sainton found only three with manifest glycosuria, and these cases were complicated by hypophyseal and suprarenal disturbances. Thompson found three cases out of 80, and Billings 1 out of 61 cases. Kocher declared that he had never met with a single example of diabetes among the numerous patients on whom he had operated for exophthalmic goitre. Gastaud, who collected 58 cases of the association of the two diseases in 1913, estimates that 3 per cent. of cases of exophthalmic goitre are accompanied by diabetes. The association is commonest in the female sex, and the age of its occurrence is usually between 40 and 60. The mortality, as might be expected, is far higher than in simple Graves's disease.

Williamson records numerous cases illustrating the relation of Graves's disease to diabetes and glycosuria and groups them as follows: (1) Graves's disease followed by or associated with mild or well-marked diabetes. (2) The occurrence of temporary or intermittent slight glycosuria in Graves's disease. (3) Mild diabetes followed by Graves's disease—a very rare occurrence. (4) Graves's disease and alimentary glycosuria. The administration of a large quantity of sugar is much more likely to give rise to alimentary glycosuria in the subjects of Graves's disease than in normal persons. (5) The occurrence of Graves's disease and diabetes after a sudden mental shock or great mental anxiety. (6) Family history of diabetes in cases of Graves's disease. (7) Graves's disease and acetonaemia. Occasionally symptoms of acetonaemia may occur in Graves's disease and the urine may show a marked diacetic acid reaction, though there is no sugar. According to Labbé (1), who records 5 cases, the association is not a mere coincidence, but the diabetes appears to be the result of a functional disturbance of the thyroid gland. Instances have been recorded by Manby, Lancereaux, and Pribram of the two diseases occurring at the same time in several members of the same family, thus proving the existence of a morbid relationship between diabetes and exophthalmic goitre. All forms of diabetes may occur. Sometimes the disease is severe and accompanied by loss of nutrition and acidosis: in several cases the patient has died of diabetic coma, in others the acidosis is intermittent. In the milder forms there is no acidosis. On the other hand, intense and early acidosis may occur with less disturbance of the regulation of sugar. There are moderate attacks of diabetes in which the glycosuria is slight and transitory and not accompanied by other symptoms of hyperglycaemia. The special features of diabetes in exophthalmic goitre are that the glycosuria is more resistant and less affected by the diet than in uncomplicated diabetes. It may often appear or disappear without any known cause. Sometimes the exacerbation of diabetes is definitely related to that of the exophthalmic goitre, the glycosuria appearing at the same time as the goitre and the diabetes becoming worse if the goitre assumes the character of Graves's disease.

Diabetes and war. At a meeting of the Berlin Society for Internal Medicine on October 20 Magnus-Levy stated that in the years immediately preceding the war the number of deaths from diabetes in Berlin remained constant, whereas during the last four years it had constantly fallen, being 202 as compared with 444 in the four years preceding the war. The male sex showed a greater decline in the mortality than the female. 75 per cent. of the deaths occurred above 50 years of age. It was a remarkable fact that the percentage mortality among children had sunk as low as in adults. Mistakes in diagnosis could not account for the diminished mortality either in children or in adults. It was, on the contrary, more probable that the diabetes mortality was still lower because patients who died of intercurrent diseases counted as diabetics to the end of their lives owing to their food cards. Cases of severe diabetes suffered most from the food restrictions, but Magnus-Levy's impression was that they did not die sooner than in peace time. Coma and acidosis were less frequent, while the development of tuberculosis was decidedly more common. The experience of a diminution in diabetes, as the result of a blockade, had already been made during the Siege of Paris. In this connexion it is interesting to note that during the German occupation of Lille many cases of glycosuria improved or recovered spontaneously as the mere result of the scarcity of food (Laguesse).

Magnus-Levy's paper was discussed by His, Brugsch, and Hirschfeld, His remarking that one of the most striking occurrences was the fact that no case of diabetes had been observed as the result of cerebral concussion. The cases of diabetes which did occur in the war were found in men who by reason of their age and constitution would have been liable to have developed it just as much in peace time, and usually did not belong to the fighting forces at all. Although aggravation of pre-existing or even latent diabetes by trauma was sufficiently proved, His contested the existence of a primary diabetes of traumatic origin. Brugsch agreed that only a very few cases of so-called traumatic diabetes were really due to trauma. The only form to which he did assign a traumatic character was the pituitary form of diabetes which developed very soon after a trauma, and was characterized by a high degree of polyuria. This form of true traumatic diabetes was not to be attributed to disease of the islands of Langerhans, but to morbid processes at the base of the brain, probably in the subthalamic region. Hirschfeld stated that a relatively trivial injury to a pancreas which was only slightly inflamed, or in which the inflammation had recently subsided, might cause a recrudescence of the process and considerable persistence of glycosuria. Magnus-Levy, in concluding the discussion, said that apart from the very rare cases mentioned by Brugsch, a form of traumatic diabetes might occur usually after head injuries, but almost always completely subsided in a few weeks. The existence of a permanent post-traumatic diabetes was disproved by scientific investigation. In spite of the innumerable physical and moral shocks which had occurred in the war, no instance of recent diabetes attributable to them had been observed, although there were many predisposed persons among the older officers and men.

Horowitz reports three cases of **juvenile diabetes**, the patients being aged 3 years, 2 years and 8 months, and 2 years respectively. In two cases there was a definite history of intestinal toxaemia immediately preceding the disease. One died and two recovered, one of the latter being a twin, whose twin sister had died of diabetes. These cases show that diabetes in children is not necessarily fatal, but that if they can be tided over a certain length of time they will outgrow the tendency completely. In one case the Allen method was used up to the sixth day, when the child became semi-comatose and the treatment had to be changed. In the other two cases the patients were treated by restricted diet instead of starvation, and trained to eat and tolerate green vegetables with little or no discomfort.

The subject of **pancreatic diabetes** is discussed by Labbé (2) who, in order to determine the pathogenic significance of lesions of the pancreas, in conjunction with Laignel-Lavastine and Vitry made a histological study of this organ in 19 cases of diabetes and in 37 cases of other diseases. Like other observers they usually found in the diabetic cases a rarefaction and lesions of the islands of Langerhans, but this general rule was by no means without exceptions. In several instances the pancreas in severe diabetes showed numerous healthy islands of Langerhans, so that there was no relation between the intensity of the lesions in the pancreas and the severity of the diabetes. On the other hand, examination of the pancreas in non-diabetic subjects showed in 30 out of 37 cases serious lesions affecting either the acini or the islands of Langerhans, so that this finding was sufficient to deprive the lesions described in diabetic patients of any specific character. But Labbé points out that though all forms of diabetes do not originate in the pancreas, certain forms are undoubtedly due to a change in this organ, such as sclerosis, lithiasis, or cancer, which give rise to a loss of function in the gland. These cases, for which Labbé reserves the term of pancreatic diabetes, are characterized clinically by a loss of the internal secretion and consequent diabetes and by a loss of the normal secretion which causes digestive disturbances.

The diabetic syndrome may occur in various degrees, (1) as mild transient glycosuria, (2) as permanent and considerable glycosuria but curable by an appropriate regimen. The hyperglycaemia is sometimes accompanied by other symptoms, e.g. polydipsia, polyuria, loosening of the teeth, and suppuration, (3) as severe diabetes with loss of nitrogenous nutrition and acidosis. The digestive syndrome is characterized by dyspepsia and the evacuation of abundant, soft, fatty stools. Owing to defective absorption rapid and profound emaciation takes place, accompanied by general debility. Pain is an inconstant feature, and usually occurs in the form of violent colic situated in the epigastrium and radiating to the hypochondrium, back and right shoulder. It is distinguished from hepatic colic, for which it is apt to be mistaken by the absence of jaundice. The anatomical lesions in pancreatic diabetes are represented in most cases by sclerotic pancreatitis or lithiasis, and occasionally by cancer. Syphilis has been incriminated in a few doubtful cases (*vide supra*). No tuberculous lesions in the pancreas have hitherto been found at the autopsy on a diabetic subject. The diagnosis of pancreatic diabetes cannot be made by the form or intensity of the diabetic syndrome, but only by the insufficiency of the external and internal secretions of the pancreas. The prognosis of pancreatic diabetes is always grave. Although its course is not invariably rapid, it is continuous and progressive, and the association of the diabetic and digestive syndromes soon leads to a state of emaciation, weakness, and cachexia.

In his thesis on the **stomatology** of diabetes mellitus Poiré describes the following changes likely to be met with in this disease: (1) Perlèche or fissures of the labial commissures. As a rule this condition, which does not run such an acute course as in children, is found in untreated cases. It appears to be caused by numerous organisms, among which the fuso-spirillar symbiosis of Vincent predominates, and is due to the thirsty diabetic patient frequently moistening his lips with the tip of his tongue, thereby causing a maceration of the labial commissures which thus afford a suitable soil for the development of micro-organisms. (2) The soft palate at the onset of diabetes presents a characteristic carmine pink appearance, which is particularly marked in patients who have had no treatment or who have discontinued it for some time. The same colouration is present, though less frequently, on the tongue. (3) The buccal lesions of diabetes consist of chronic gingivitis. Lactic acid plays an active part in the decalcification of the cement, thereby causing loosening and loss of the teeth. Owing to its acidity the saliva of the diabetic patient favours the increase of micro-organisms, especially of Vincent's bacilli, but prevents the development of anaerobes, as is shown by the absence of foetor in the gingivo-dental abscesses in diabetes. Poiré concludes that it is possible, by the mere examination of the mouth, to diagnose diabetes in a patient who seeks advice for his buccal symptoms.

Blood-sugar. In a paper on estimations of sugar in the blood in the diagnosis and treatment of diabetes Cammidge (1) points out that in a normal person a maximum percentage of blood-sugar should be found at about the third hour after a meal and should not be higher than 0·15 per cent. Any excess in this figure and a delay beyond the fifth hour in the fall to 0·10 per cent. show that the carbohydrate metabolism is defective, and that the patient must at least be classed as a potential diabetic. With increasing severity of the defect in carbohydrate metabolism the deviations from the normal in the time and space relations of the sugar curve become more and more pronounced until a permanent hyperglycaemia is established. A meal containing only a moderate amount of starch will then send the blood-sugar up to 0·40 or 0·50 per cent. or more. From a study of over 700 cases of diabetes Cammidge has found that there is no constant blood-sugar level for the appearance of sugar in the urine in quantities recognizable by ordinary tests, and that there is no definite relationship between the percentage of sugar in the blood and either the percentage or total amount of sugar excreted by the kidneys. As a rule young diabetics have a lower threshold point for clinical glycosuria than those of middle age, and the threshold rises with advancing years. It is therefore important that the presence of even small amounts of sugar in the urine of middle-aged persons should not be dismissed as of little significance unless blood-tests have shown them that their tolerance for carbohydrate is not seriously defective. A comparatively low blood-sugar content is usually a good sign in ordinary frank diabetes, even when a large amount of sugar is being passed in the urine. On the other hand, a progressively rising blood-sugar is a serious prognostic sign, and suggests the need for an immediate revision of the diet even when the urine is free from sugar.

Friedlaender of Breslau records a fatal case of diabetes mellitus in a man aged 22, remarkable for its rapid course (three weeks) and for the extraordinary high amount of blood-sugar, viz., 1·03 per cent. The highest amount of blood-sugar ever found by von Noorden was 1·01 per cent. Lepine found the still higher amount of 1·06 per cent. in a woman of 69, who died in coma, and Sohn reports a case which died with a blood-sugar content of 1·96 per cent. In Friedlaender's case there was no acidosis, and apart from a moderate degree of colitis no morbid changes were found in the organs *post mortem,* the kidneys, suprarenals, pancreas, brain, and hypophysis being completely normal both on naked eye and microscopical examination. Friedlaender thinks that the atypical coma in which the patient died was caused by an excess of sugar in the organism and direct damage to the central nervous system.

Lindblom, on the other hand, regards hyperglycaemia as a not altogether harmful factor in diabetes, and he compares it with the high blood-pressure of arteriosclerosis. Just as a high blood-pressure may aid the circulation of blood through rigid vessels, so hyperglycaemia may help to restore the sugar equilibrium in the body by stimulating the mechanism that inhibits the production and favours the destruction of sugar in an organism incapable of responding in these directions to normal glycaemia. Following up this comparison, he observes that, just as a high blood-pressure eventually is harmful by promoting arteriosclerosis, so the hyperglycaemia of diabetes may exhaust the mechanism regulating the sugar equilibrium, an increasing concentration of sugar in the blood being required to stimulate this mechanism into activity. He suggests that hyperglycaemia may be beneficial in gradually decreasing the permeability of the kidneys to sugar, and that the freedom from glycosuria achieved by some diabetics may be because of, not in spite of, the persistence of hyperglycaemia. This is injurious in so far as it (1) blunts the mechanism by which, in response to the stimulus of glycaemia, the production and destruction of sugar in the body are regulated, and (2) it promotes cataract, gangrene, furunculosis, &c. Further, it is the measure of the degree of blunting of the sugar-regulation mechanism. On the other hand, hypoglycaemia may be indicative of abnormal excitability of this mechanism. If the concentration of sugar in the blood can be reduced, this mechanism is rested, and its responsiveness to the stimulus of sugar in the blood increased. Hence the beneficial effect of a carbohydrate free diet, although it deprives the body of the partially beneficial stimulus of hyperglycaemia. Lindblom suggests that his hypotheses may account for the good effects of an oatmeal regimen in diabetes. The organism being flooded with carbohydrates, and hyperglycaemia provoked, a powerful stimulus is given which, for a time at any rate, stirs into useful activity the mechanism controlling the sugar metabolism. Lindblom's speculations have as their foundation a series of investigations recently published in Stockholm by George Engstrand. Lindblom qualifies his appreciation of these important and laborious investigations by an interpretation of their significance at variance with Engstrand.

Chauffard and Grigaud draw attention to the dehydration of the blood and organs which occurs in diabetic coma. The blood increases in viscosity and density, the skin becomes cyanosed and flaccid, the eyeballs sunken, the pulse small and feeble, and the blood-pressure very low. On post-mortem examination the coefficient of dehydration varies with the different organs, but the pancreas is always most affected. The pathological physiology of the process is obscure. In none of the writers' cases was the dehydration associated with a sclerotic state of the gland. It is undoubtedly

MEDICAL RESEARCH COUNCIL.

National Collection of Type Cultures.

(Lister Institute, Chelsea Gardens, London, S.W.)

28th May, 1920.

The Medical Research Committee (now the Medical Research Council) have long had in view the formation of a National Collection of Type Cultures, from which biologists in general and bacteriologists in particular may obtain from a trustworthy source authentic strains of recognized bacteria and protozoa for use in scientific work. The need of an available supply of this kind has long been felt in many directions and particularly in medical research work, for the study of principles and methods in bacteriological technique and for the systematic classification of bacteria and protozoa in their various species and strains.

In the past the needs of workers in this respect have never been fully met. In this country the Lister Institute of Preventive Medicine has for many years assisted bacteriologists both at home and abroad, so far as the resources of its own private collection have permitted, but British workers have been dependent in great part upon the courtesy of scientific colleagues or upon the collections of Institutes in other countries. Before the war the collection at the Pasteur Institute in Paris, maintained by M. Binot, was very helpful to workers here. A collection of type cultures was formerly maintained on a commercial basis by Král at Prague, and this was subsequently transferred to the Sero-physiological Institute of Vienna. This source of supply was never completely satisfactory, though many made use of it. In America the Museum of Natural History in New York has maintained a Culture Bureau during the last eight years, and it is believed that the activities of the Bureau have been of the greatest benefit to workers there, not only by the provision of authentic cultures, but also by the studies in classification made by its staff. Early in the present year the Medical Research Council were able, by the courtesy of the Governing Body of the Lister Institute, to make arrangements to maintain a National Collection of Type Cultures at the Institute, where all the necessary facilities have been provided. The scheme will be under the general direction, on behalf of the Council, of Dr. J. C. G. Ledingham, a member of the staff of the Lister Institute, while Dr. R. St. John Brooks and Miss M. Rhodes have been appointed by the Council to be Curator and Assistant Curator respectively. The Medical Research Council are greatly indebted to the Governing Body for this opportunity of establishing a central collection upon a proper footing at once, without further delay. The present arrangement is made for a short term of years, before the end of which the future location of the collection will be considered.

It is proposed to collect and maintain bacterial and protozoal strains of medical, veterinary, and economic importance, but in the immediate future the efforts of the staff will be directed more particularly to obtaining fully authenticated strains of pathogenic organisms.

Subsidiary researches on the viability of bacteria in artificial media will be undertaken with a view to the discovery of economical and labour-saving methods of sub-culture. The staff will also be prepared to give help in the identification and classification of strains received from workers at home or abroad.

The co-operation of bacteriologists is earnestly invited, and in return every effort will be made to supply the needs of applicants for cultures. Cultures that may be sent either for identification or for maintenance in the collection should be accompanied by the fullest particulars as to source and date of isolation and, if possible, by clinical and epidemiological notes. It must naturally be left to the discretion of the Director to decide whether given cultures are of sufficient importance to be maintained in the collection, but it is hoped that this will not deter workers from forwarding strains of even the commonest types of organism. These will have value in view of the necessity of maintaining an adequate representation of strains of recent origin. Studies in classification will also be aided if large series of authentic specimens of closely related species are available for workers.

Cultures will be supplied on demand so far as possible to workers at home or abroad and, as a rule, a small charge will be made to defray the cost of media and postage. Strains representing at least the commoner types of human infection can already be supplied, and at a later date it is proposed to prepare a catalogue for publication.

It is requested that all communications be addressed to
THE CURATOR, NATIONAL COLLECTION OF TYPE CULTURES,
LISTER INSTITUTE, CHELSEA GARDENS, LONDON, S.W. 1.

diabetic coma and not diabetes alone which is responsible, as in a severe case of diabetes in which death was due to pulmonary tuberculosis the water content of the pancreas was raised instead of lowered. The writers conclude that dehydration of the pancreas in diabetic coma represents a terminal exhaustion of the gland associated with a more or less complete disappearance of water in the tissues.

Weil, who is attached to Strauss's Clinique in Berlin, distinguishes three possible combinations of **albuminuria and diabetes**: (1) A harmless albuminuria associated with glycosuria, which clears up as the sugar in the urine disappears or is greatly diminished (saccharogenous albuminuria of Strauss). (2) Albuminuria caused by the supervention of arteriosclerosis (nephrosclerosis diabetica). (3) Albuminuria caused by actual nephritis (nephritis or nephrosis diabetica). He records five cases of diabetes associated with renal sclerosis in which functional tests of the kidney were performed, and concludes that the diagnosis and prognosis of renal sclerosis in diabetes are the same as in the absence of diabetes, and urges that in renal complications of diabetes functional tests should be employed more frequently than has hitherto been done.

Renal diabetes. Under the title of 'Diabetes innocens in young persons with remarks on renal diabetes' Salomon of Vienna in 1914 published a number of cases, the great majority of which resembled renal diabetes. The remarkable features of his cases were the long period during which they had been under observation, their frequently familial character, and the distinctness of the clinical picture which at once enabled a diagnosis and prognosis to be made. The harmless character of the cases, as Salomon shows in a recent paper, has been further proved by the fact that since 1914 the disease has not made any progress in any of the patients. The characteristic features of these cases of innocent or renal diabetes is the continual excretion of small percentages of sugar which are subject to only slight variations in spite of the greatest changes in the carbohydrate content of the food. This small percentage of sugar, however, cannot be made to disappear even on the strictest diet. In rare cases a mild form of albuminuria or even haematuria appears. The fasting blood-sugar is usually normal, but in rare cases is increased in amount. Alimentary hyperglycaemia is usually absent, but its presence does not negative the existence of diabetes innocens. Owing to the close resemblance of this type to true diabetes Salomon considers that the prognosis should be reserved for a considerable time. The occurrence of diabetes innocens in other members of the family is strongly in favour of the diagnosis in a given case. There is a rare form of diabetes innocens characterized by a high percentage of sugar excretion, the amount in some of Salomon's cases being as high as 3 per cent., and the amount excreted daily 40 gm. In such cases, apart from the family history and the favourable course of the individual case, the determination of blood-sugar will be a guide (absence of fasting and alimentary hyperglycaemia). Occasionally instances of transient and intermittent diabetes innocens occur, e. g. in pregnancy or on administration of thyroid extract.

The occurrence of hereditary and familial renal diabetes is discussed by Brugsch and Dresel, who publish a pedigree showing that of 55 descendants 13 at least were diabetics, and probably the real number was still higher. In the case of the father and three daughters, aged 17, 15, and 7 years, respectively examined by the writers, the excretion of sugar was always within moderate limits, hardly ever exceeding 1 per cent. in the urine, while the blood-sugar was below 0·1 per cent. and was quite independent of the food. The cases corresponded in all respects with those described as renal diabetes: (1) The total excretion of sugar did not exceed 10 gm. (2) The glycosuria was quite independent of the diet. (3) The blood-sugar value was normal. Addition of carbohydrates to the diet did not increase the blood-sugar content. (4) Persistence of the condition for many years without change (in 1 case for over 18 years, and in the rest up to 11 years). (5) Well-marked hereditary and familial character.

Allen, Wishart, and Smith record 3 cases of renal glycosuria which occurred among a total of 40 cases of supposed diabetes in a military hospital, from which they conclude that renal glycosuria is not so rare as was once supposed, and is probably much commoner than other anomalies such as pentosuria and laevulosuria. Cammidge (1) regards renal diabetes as probably a congenital abnormality depending upon an abnormal permeability of the kidneys for sugar. Restriction of the diet in his opinion is unnecessary and does more harm than good, as it renders the patient less able to withstand prolonged physical exercise. Two of his cases occurred in a father and daughter.

Diabetes insipidus. Pagniez points out the following close relations between diabetes insipidus and the hypophysis. In a certain number of cases of diabetes insipidus there is a lesion of the hypophysis which has sometimes been recognized during life by the X-rays showing a widening of the sella turcica, or has been manifested by signs of compression of the chiasma. The nature of the lesion may vary. It may be a secondary cancerous growth (Simmonds, Rosenhaupt), or tubercle of the hypophysis (Hausalter and Lucien). In Claude and Lhermitte's case there was a cystic tumour behind the chiasma and the hypophysis was quite intact. Clinically the syndrome of diabetes insipidus may exist by itself, but it may be associated with other symptoms indicating a lesion of the hypophysis or its neighbourhood. Thus it has been found in cases of dwarfism or infantilism of the pituitary type and in the adiposo-genital syndrome in the child. In 1913 Farini was the first to show that the polyuria of diabetes insipidus, which had hitherto been refractory to all treatment, was immediately modified by injection of pituitary extract, and numerous other observers have since confirmed this. In all cases this injection causes a considerable diminution in the amount of the urine, and in some cases reduces it to normal. The oliguria produced by injection of pituitary extract in diabetes insipidus appears to be quite specific, as no other glandular extract possesses a similar property. It should be noted that it is only the posterior part of the hypophysis which furnishes an active extract, and that injection alone has any effect, the polyuria not being influenced when the extract is given by mouth.

According to von Hann, quoted by Neubürger, destruction of the posterior lobe of the hypophysis is not sufficient in itself to cause diabetes insipidus, this condition being due to the coexistence of an intact or at all events an active anterior lobe. The latter possesses a diuretic action, whereas the posterior lobe has an antidiuretic action. When the function of the posterior lobe fails an increased diuresis takes place, but if the anterior lobe is affected this action is impossible. In confirmation of von Hann's view Neubürger records a case of mammary cancer and diabetes insipidus in a woman aged 51, with metastases in the posterior lobe of the hypophysis. The anterior lobe was almost entirely intact and was undoubtedly still functionally active in a high degree. In another two cases of mammary cancer, in which there were metastases in the posterior lobe, the growths were very small, and no symptoms of diabetes insipidus developed.

Cowie records a case of idiopathic diabetes insipidus in a girl aged 10 years. Syphilis and tuberculosis could be excluded as aetiological factors, and there was no history of injury. Skiagrams were negative, and the epinephrin and blood-sugar curves were normal.

Treatment. Owing to the importance of bringing diabetic patients under treatment early Hoogslag makes the following proposals: (1) Every general practitioner, specialist, and dentist should examine the urine of every patient, irrespective of age, sex, or complaint. (2) Whenever a case of diabetes occurs in a family the doctor should insist on examining the urine of each member of the family yearly. (3) Life insurance societies should make arrangements for all policy-holders to have their urine examined free of charge yearly.

In a paper on the treatment of diabetes mellitus in children and adolescents Leyton (1) emphasizes the importance of freeing the patient from any infection, especially in the nose, throat, or skin, before attempting to find the optimum diet. He states that children stand the Allen treatment excellently, and are quite tractable provided they are removed from their parents and their most sympathetic friends and nurses to a hospital or nursing home. On admission the patient is put on a diet consisting of small quantities of carbohydrate and protein with a minimum quantity of fat for two days. After the urine has been free from sugar for 24 hours, a small quantity of fat is given in the form of vegetable. The optimum diet is one containing two-thirds of the limit of carbohydrate tolerance, 2 gm. of protein per kilogram weight, and sufficient fat to make the energy of the diet equal to 60 calories per kilogram body weight.

Stillman, of the Hospital of the Rockefeller Institute for Medical Research, classifies diabetic patients into four groups, according to their tendencies to develop acidosis, and assigns the following more or less typical treatment to each group. The first group, which constituted 46·8 per cent. of the cases, showed no tendency to acidosis either on fast or ordinary diet regardless of the degree of glycosuria. These cases were safely made aglycosuric by a continuous fast, and could usually be made to tolerate fairly high calory diet without glycosuria or ketonuria. The second group, which formed 32·3 per cent. of the cases, were admitted in a condition of moderate or severe acidosis. They were made free of glycosuria and acidosis by a continuous fast, but a tendency to acidosis was always present, and a safely tolerated maintenance diet was usually lower than in the first group. The third group, which formed 14·5 per cent. of the cases, showed a tendency to slight acidosis on all but the most carefully chosen diet. The glycosuria in these cases was removed by a continuous fast. The fourth group, which formed 6·4 per cent. of the cases, either developed or retained severe acidosis when fasting was instituted. In such cases an intermittent had to be substituted for a continuous fast.

Geyelin, of New York, states that the high fat feeding of former years has led to more fatal outcomes in diabetes than any other factor. He thinks that coma may be averted in almost every case, even in the presence of infections, provided the fat of the food is kept at the proper level or in extreme instances totally eliminated. At the Presbyterian Hospital, New York, during 1912, 1913, and 1914, all the patients were treated by the old method. During 1915 most of the patients were treated by the old method, but some were treated by the modern method. From 1916 to 1919 all the patients received the newer treatment. In spite of the greatly increased number of diabetic patients, the mortality which formerly had ranged from 13·5 to 37·5 per cent. dropped to 5·0 to 12·6 per cent. There had also been proportionately fewer deaths from coma during the past three and a half years. The most striking feature was the great increase in the number of patients discharged free from sugar and ketone bodies. The effect of the modern treatment on surgical conditions associated with diabetes was shown by the results of combined medical and surgical treatment, being much better than with the previous method of treatment.

Having had experience of about 50 cases treated by the Allen method, each of which was under observation over two years, Stark, of New York, regards the fasting treatment as of doubtful value, though he does not deny that it can usually be relied upon to make the diabetic temporarily sugar-free. He found that some patients bore the initial fast very badly and showed evidence of stomach catarrh or colitis, or even symptoms referable to the liver or pancreas. Another group of patients showed signs of increasing acidosis or impending coma. There was yet another group who stood the initial fast apparently without harm, and were then allowed small amounts of carbohydrates, whereupon they developed a much more severe acidosis than before. Fasting was better borne and there was less tendency to acidosis of a severe type in thin subjects than in obese ones. Children bore fasting well, but required a relatively greater caloric intake than adults.

According to Strauss, chronic underfeeding as a curative agent in diabetes, especially in mild and moderate forms, was recommended a hundred years ago by Prout, and Bouchardat from his experience during the Siege of Paris advised that 'Mangez le moins possible' should be the principle of the treatment of diabetes. Strauss found that the protracted fast cures recommended by American writers caused such a rapid fall of weight and made the patients feel so miserable that he did not try the treatment in more than four cases. On the other hand he is convinced of the value of 'drink days' in which the diet is confined for 36 hours to fluids in the form of water, tea, coffee, wine, cognac, and bouillon, with or without the addition of very small amounts of food deficient in carbohydrate and albumin. The effect of this diet is not only to reduce the glycosuria but also the excretion of acetone. He therefore recommends that fasting or drink days should be used much more in the treatment of obstinate cases of diabetes than has hitherto been the case.

For several years Le Noir has adopted a **milk cure** in the treatment of diabetes not only in severe complications as is generally recommended, but also as an occasional interruption in a diet of meat and fat which, if long continued, cannot fail to have bad results. The patients are given 2–3 litres of milk a day as their sole diet for a period of five days. A loss of weight occurs but is not excessive. The treatment should be repeated at longer or shorter intervals according to the severity of the case, the tendency to visceral complications, changes in the arterial system, &c. Out of 17 cases so treated the sugar completely disappeared in four after the first cure and did not reappear except in slight traces for several months; in nine cases the sugar diminished considerably after each cure, often by as much as two-thirds or a half, and in four cases the amount of sugar remained the same or increased. Four-fifths therefore of the patients were benefited as regards their glycosuria and also as regards their general condition.

As the result of experiments with commonly used vegetables, Cammidge (2) found that after three boilings celery, rhubarb, spinach, sliced turnip and carrot became free of carbohydrate. Even when thrice boiled vegetables were not quite free of carbohydrate, the percentage was so much reduced that from four to thirty times as much of the thrice boiled as of the once boiled material would contain the same amount of carbohydrate. Repeated boilings, however, considerably impaired the flavour and appearance of the vegetables, and it was found that a more tempting and equally carbohydrate-free product could be prepared from some vegetables by repeated extraction at a temperature considerably below the boiling point of water (60°C.). The extracted vegetables could be preserved for future use by desiccation in a current of air from an electric fan for 3½ hours, and when required could be prepared for use by soaking in water and re-heating.

In a discussion on the value of **alcohol** as a therapeutic agent at the Section of Therapeutics and Pharmacology of the Royal Society of Medicine, Leyton (2) stated that in diabetes it was his custom to order alcohol as a foodstuff during the period of very meagre diet to those patients who had been accustomed to take alcohol. The advantages of this were first the supply of a small amount of energy, and secondly the patients were less irritable and were able to stand the treatment better. He had come to the conclusion that alcohol was a necessity in some of the more advanced cases of diabetes mellitus, and he had found patients who had maintained their weight on taking alcohol but who had lost weight after they had stopped taking it, the diet having been maintained constant in every other respect.

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MALARIA

Epidemiology. It is generally agreed that the endemic index which is established either by examination of blood films or by palpation of the spleen is the only scientific method of obtaining an exact idea of the prevalence of malaria in a country. Porry, who has devoted his Paris thesis to the study of the endemic index in the French colonies, states that Corsica has a high endemic index during the summer and autumn, viz. 28 per cent. before and 42 per cent. during the hot season. The disease, however, is disappearing and the interior of the island is healthy. The French colonies in Africa are those in which malaria is most prevalent, the endemic index being 40 per. cent. in Algeria, 45 per cent. on the Ivory Coast, 60 per cent. in Senegal, 77 per cent. in the Gaboon, and over 97 per cent. in Timbuctoo and the adjoining region. In Indo-China malaria is not the principal disease. Apart from certain localities such as the Black River where the endemic index is 42 per cent., Tonkin has an index ranging from 2–10 per cent.; in Annam very unhealthy regions adjoin others in which the index is nil. In the West Indies there are two healthy colonies, viz. Guadeloupe and Martinique, in which the index is only 2·69 per cent. and one unhealthy colony, Guiana, in which the average index is 17 per cent.

The recent increase in the incidence of malaria in Belgium is attributed by Firket to three causes: (1) The recrudescence of malaria formerly prevalent in Flanders mainly as the result of the flooding of a large part of the Yser and Moeris meadows for strategic purposes. All the cases of this kind which occurred among Belgian soldiers were examples of benign tertian. (2) The return to Belgium of soldiers who belonged to the African Expeditionary Force. The form of malaria in these cases was malignant tertian. (3) The return of soldiers who had contracted malaria during their imprisonment in Germany and elsewhere, either by prolonged contact with carriers in concentration camps or by living in areas of indigenous malaria such as Embden, as in the two cases reported by Firket.

At the Société de Pathologie Exotique on November 12, Roblin reported an outbreak of indigenous malaria at Noyen-sur-Seine due to anophelines infected by a malarial soldier repatriated from the East. The cases were mild and due to *Plasmodium vivax*. The *Plasmodium falciparum* was not found in any case.

In the subsequent discussion Brumpt stated that he had recently seen 20 cases of indigenous malaria which were also of the benign tertian type in the Seine and Marne district.

Owing to the relative scarcity of anophelines in the Berlin district, and especially in the town itself, very few cases of malaria have occurred in Berlin in spite of the expectation that the disease would be widely disseminated as the result of the war. Only a few cases have been recorded by Stadelmann and Umber in 1917, and Retzlaff now reports a case of benign tertian in a man who had never left Berlin.

On the other hand, in an article published on January 19, Schäfer records three cases to show that the dissemination of malaria in Germany at the present time is much greater than is generally supposed. The cases are often examples of relapses or of larval malaria, the patients themselves not being aware of their disease.

Huntemüller has seen a large number of soldiers who first developed malaria after their return to Berlin from a malarious district in Russia where they had never fallen ill in spite of not taking quinine. He also found that numerous cases of malaria developed in Germany among soldiers who had returned from the Macedonian front, where they had had a very vigorous prophylactic treatment. The cases proved very refractory to quinine treatment, so that he concluded that the taking of quinine for a long period, especially in large doses, had a bad effect upon the system and lowered its power of resistance.

Like Flebbe (vide *Med. Science*, 1919, **1**, 63) and Bentmann (*ibid.*, 260) Schilling emphasizes the severe endemic character of malaria in Cilicia, Taurus and Amanus in 1916. Under circumstances connected with the war and the climatic conditions it assumed a still more virulent and malignant character. Many cases, whether they had had quinine prophylaxis or not, showed from the first a relative resistance to the ordinary therapeutical doses of quinine, though an absolute resistance was present in only a few instances. According to the registers of the Belemedik Hospital the mortality of the malaria admissions in 1916 was 51 per cent. in August, 27 per cent. in September, 22 per cent. in November, 16 per cent. in December, 1·7 per cent. in January and February 1917, 6·3 per cent. in March, and 4 per cent. in April. The appallingly high mortality was explained by the absence of microscopical control, the bad state of the patients on admission, and the indifference of the native practitioners. Under proper diagnosis, prophylaxis, and treatment the number of malaria admissions considerably increased, but the mortality sank to a more normal level, except when the patients were admitted too late, the figures for May 1917 to February 1918 ranging from 1·1 to 7·2 per cent.

Symptomatology. Manson-Bahr in the account of his experiences of malaria in the Egyptian Expeditionary Force classifies the clinical symptoms of malignant malaria as follows: (1) Pernicious or rapidly fatal forms: (*a*) cerebral (generally occurring in the summer). These were liable to be mistaken for sunstroke, heatstroke, mental derangement, epilepsy or cerebrospinal meningitis. (*b*) Abdominal (generally occurring in the winter) simulating dysentery, cholera, intestinal obstruction, appendicitis or cholecystitis. (*c*) Pulmonary, diagnosed as bronchitis, pneumonia or pleurisy. (*d*) Cases with skin lesions mistaken for purpura or measles. (2) Clinical types of average severity; (*a*) Influenzal or myalgic. (*b*) Enteric, with steppage rise of temperature. (*c*) Icteric with bilious vomit. (*d*) Nephritic. (3) Sequelae: (*a*) Cachexia and anaemia. (*b*) Blackwater fever.

In a paper on **apyrexial symptoms in malaria** Ward states that the following signs and symptoms constitute a syndrome which is not met with in any other disease, although trench fever presents many of them: (*a*) Rigor, hot stage, sweating. (*b*) Periodicity of symptoms or pyrexia. (*c*) Perisplenitis. When the spleen is not palpable, some abnormality may be detected on auscultation, a friction sound being heard in the sixth or seventh intercostal space. (*d*) Pain in the side confirmed by the presence of hyperalgesic areas. (*e*) Headache, especially supraorbital, similarly confirmed. (*f*) Pharyngitis and conjunctivitis which are apt to be mistaken for influenzal manifestations. (*g*) A chronic tendency to hyperidrosis. (*h*) Pigmentation, especially of the border of the red part of the lips. (*i*) Raynaud's symptoms in the form of 'dead fingers' or 'cold feet'. (*j*) Transient oedema, not necessarily accompanied by pitting, and sometimes resembling a giant urticaria. (*k*) Parasites in the blood. (*l*) Pigmented cells, excess of transitional or eosinophil cells, endothelial cells and polychrome cells of abnormal size in the blood. (*m*) Tremor of the tongue, hands, and rarely of the lips. (*n*) Herpes labialis. (*o*) Jaundice. (*p*) Tachycardia, usually most marked when the patient gets up for the first time. (*q*) Weakness shown by flabbiness of muscles and general want of tone, dyspnoea on exertion, &c. These phenomena are all wholly or partially out of the patient's control, and the presence of several of them may be regarded as strong evidence in support of his statement that they are the result of malaria.

Gutmann and Porak describe various hypothermic forms of malaria. In some cases the temperature is persistently subnormal, remaining for weeks at about 96·8, and often the patients do not complain of any special symptoms. In other cases typical malarial paroxysms or attacks of continued fever which it is difficult to diagnose are followed by a period of subnormal temperature. A study of the temperature charts, however, shows certain characteristic features of malaria, e. g. very abortive attacks, the temperature presenting either a periodical rise from subnormal to 98·6 or just above, or a periodical fall from 98·6 or 96·8 to 95°. These abortive forms are accompanied by other malarial manifestations, e. g. enlargement of the spleen, definite rise of blood-pressure, and malarial psychoses, which as the writers have shown, usually occur without a rise of temperature (vide *Medical Supplement*, 1918, **1**, 143 *a*). Moreover, the blood may be found swarming with malarial parasites which are often more numerous than in frank malarial paroxysms. The writers are of opinion that these hypothermic forms are due to insufficient treatment.

Unusual symptoms of malaria in the circulatory, respiratory, excretory, and alimentary systems are described by Carnalt Jones, who points out that malaria is one of the many contributory causes of disordered action of the heart. Apart from cases of concurrent influenza and malaria respiratory complications of malaria were frequent in the Egyptian Expeditionary Force. Symptoms of nephritis were sometimes seen. Vascular lesions were shown by cases of bleeding from the mucous membranes of the alimentary, respiratory, and urinary tracts, into a solid organ such as the spleen, and into the eye. The writer also describes four cases of **hemiplegia** possibly due to small haemorrhages or to small emboli of parasites.

Spolverini records a case of right hemiplegia in an infant at the breast preceded by epileptiform convulsions. The liver and spleen were enlarged and numerous malignant parasites were found in the blood. Both parents were suffering from malignant tertian. The condition is attributed by Spolverini to parasitic thrombrosis, the cerebral vessels being blocked by spores, pigment masses, and endothelium.

According to Forrester malaria was by far the most important factor in the causation of **mental disease** among the British troops in Macedonia. From December 1918 to October 1919, 116 cases were admitted to the mental department of the British Salonica force with a positive malaria history. The cases were divided into two groups according as the mental symptoms were associated with an actual attack of malaria or occurred as the result of repeated attacks. The cases in the first group, which consisted of 32 cases, showed that almost any of the recognized types of psychoses could be caused by the malarial parasite, but mental confusion which occurred in 22 cases or 68·75 per cent. was the most prominent symptom. Depression was next in order of frequency with 12 cases or 37·5 per cent. In the second group which consisted of 87 cases, although any type of psychosis might be set up, mental confusion and depression were also the most prominent symptoms. Unlike the cases in the first group in which heredity played a very unimportant part, an insane heredity was present in 9 out of 24 cases of depression and in 7 out of 31 cases of confusion. Unless other causes were at work, the prognosis was always good and was concomitant with improvement in health. Forrester emphasizes the importance of removing all cases of malarial psychoses from danger of re-infection.

The **pulmonary manifestations** of malaria are discussed by Falconer, who adopts the following classification: (1) Bronchitic. (2) Pleuro-pulmonary congestion with more or less definite evidence of consolidation. (3) Massive collapse of the lung. (4) Pneumonia occurring in chronic malaria without evidence of active malaria. (5) Pleurisy, either dry or with serous or haemorrhagic effusion. Falconer concludes that although malaria is frequently complicated by pneumococcal infection, numerous cases occur in which there are notable changes in the lungs without any evidence of superadded infection. In many cases the symptoms at first are almost entirely pulmonary, and the malarial infection may be overlooked. In untreated cases there is a great liability for the lung to become secondarily infected with the development of the inflammatory changes.

Bürger, assistant at the Kiel University Medical Clinique, examined the **blood-pressure** with Riva-Rocci's instrument in a number of patients suffering from chronic tertian malaria or late relapses. He found that when the paroxysm was fully developed there was a fall of 20–30 mm. Hg below the patient's normal level. But when he took the blood-pressure during the shivering stage a rise of 20–30 mm. was almost invariably found and was followed at the height of the fever by a drop of 20–30 mm. below the normal, so that during the whole febrile attack there was an oscillation of 40–60 mm. Hg. The return to the normal level took place slowly, and in some cases was not reached even twenty-four hours after the beginning of the attack.

Stoss examined the **blood** of 53 cases of chronic tertian malaria with the following results: a day before the attack there was an absolute increase in the large mononuclears which amounted to 1,000 per cubic mm. After several attacks in succession there was a transient neutrophil leucopenia followed by a neutrophil leucocytosis, two days after the last attack. A lymphocytosis of about 5,000 per cubic mm. occurred after the attacks and lasted for about a week.

Urogenital system. Nazari of the Institute of Pathological Anatomy of the University of Rome shows that in addition to enlargement of the liver and spleen in chronic malaria the kidneys also tend to increase in size and weight. He reports 10 cases showing that the weight of these organs may be more than double the normal in chronic malaria. The enlargement of the kidneys, like that of the liver and spleen, varies from one individual to another, but bears no relation to the size of either of these organs. Though increased in size they preserve their normal shape and their consistency is not increased. The capsule can be stripped readily from the outer surface which is smooth and of normal colour. On section, apart from increase in size of the various structures, there are no naked eye changes of any kind. Microscopical examination merely shows a simple hypertrophy of the glandular tissue without any marked increase of the connective tissue or much dilatation of the vessels.

Vecchia records a case of **malarial orchitis** in an Albanian native aged 16, suffering from malignant tertian. All other causes of orchitis such as gonorrhoea, mumps, syphilis or tuberculosis could be excluded, and the inflammation immediately subsided after intravenous injection of quinine, the testis resuming its normal size in two days.

Kaufman of San Francisco emphasizes the importance of routine treatment with quinine during pregnancy to prevent abortion and miscarriage. The widespread idea that quinine is an abortifacient is erroneous. Cases which showed an intolerance for quinine by mouth even in minute doses bore intramuscular injections without any ill effects. The continuance of quinine treatment after delivery is necessary (1) to prevent re-invasion, (2) to hasten involution of the uterus, and thus prevent post-partum haemorrhage and infections, (3) to aid in permitting perineal wounds to heal better, (4) to protect the milk supply for the infant, (5) as a therapeutic test to rule out malaria in the presence of other infections, (6) to maintain normal equilibrium of the mother.

Enlargement of the thyroid gland as a complication of malaria is described by Hume who saw about 30 cases during the East African campaign among the white troops, and suffered himself from a marked enlargement of the gland during an attack of malaria. The condition is characterized by an acute enlargement of one or both lobes and occurs about 12–24 hours after the fall of the temperature. In none of the cases was there any previous personal or family history of goitre. Dysphagia was a prominent symptom. Pain and throbbing in the head were frequent. There was usually slight muscular tremor. In only two cases was there any exophthalmos. Tachycardia was very constantly present. In most cases there was a marked reduction of the swelling in from four to ten days. Hume suggests the thyroid enlargement is due to sporulation of the parasites in the capillaries of the gland, analogous to the condition in cerebral malaria. As the iodothyrin is thus cut off from the blood-stream, thyroid equilibrium is upset and hypertrophy takes place.

Malaria and enteric fever. Mixed infections of malaria and enteric fever are classified by Koch and von Lippmann as follows: (1) The enteric infection succeeds malaria after a certain interval. Quinine has no effect on the fever and malarial parasites are no longer found in the blood, but typhoid or paratyphoid bacilli are cultivated therefrom. (2) Both diseases occur simultaneously. These cases begin with a rigor and the presence of malarial parasites in the blood, but the temperature is not affected by quinine. The plasmodia soon disappear from the blood, from which typhoid or paratyphoid bacilli can be cultivated. Cases of this kind are even more likely than those of the first group to suggest resistance to quinine on the part of the malarial parasite. But the real explanation of the fever not giving way to four or five days' quinine treatment is that there is no malaria present. (3) In the course of a typhoid or paratyphoid infection young malarial parasites are found in the blood, although hitherto no clinical or microscopical evidence of malaria has been detected. This group is much rarer than either of the two preceding. (4) A hitherto latent malaria develops at the end of an attack of enteric. In such cases the enteric infection has apparently a sort of provocative action on latent malaria. (5) Latent malaria develops some time after an attack of enteric. As regards the influence which the two infections have upon one another, the common features in groups 1, 2, and 5 are that both diseases run their course without any effect upon one another. The rarity of the occurrence of young malarial parasites at the height of an attack of enteric suggests that the latter is to a certain extent able to prevent the passage of malarial parasites into the blood. In the writers' experience the prognosis of these mixed infections depends upon the character of the attack of enteric, provided that the malaria has been recognized and treated in time.

Crespin and Athias of Algiers emphasize the occasional difficulty of diagnosing between malaria and typhoid fever and record a case of brother and sister with continued fever of malarial origin in one of whom the resemblance to typhoid was increased by the occurrence of intestinal haemorrhage, a complication which the writers were informed used to occur among malarial patients at Salonica. Similar cases are also reported by Carmalt Jones.

According to Verdelet, who discusses the **surgical aspects of malaria,** the relation of malaria to wounds has been summarized by Le Dantec as follows: (1) If the wounded man is suffering from malaria or has had the disease some time ago, the wound will aggravate the attacks or hasten their recurrence; (2) if he has not yet had malaria but is living or has recently resided in a malarious country, the wound will cause the disease to develop; (3) if his parents are subject to malaria, the wound will have the same effect.

Brun, who is surgeon of the Sadiki hospital at Tunis, states that a rise of temperature after an operation to 102·2 or 104° is almost the rule in chronic malaria, and an occasional though less frequent event in patients who have previously suffered from malaria but have apparently completely recovered. This rise of temperature, which is independent of the method of anaesthesia, occurs on the evening of the operation or the next day, and is not preceded by shivering or followed by sweating, and the general condition remains good. The temperature as a rule falls to normal the following day, but sometimes a similar attack occurs on the second or third day. The rise of temperature can always be prevented by quinine. Brun's practice is to give an intramuscular injection of 1 grm. of quinine hydrochloride in every definite case of malaria on each of the two or three days following the operation.

Rowan reports a case of spontaneous rupture of a malarial spleen in a soldier aged 29. Laparotomy was performed, and the spleen, which weighed 2 lb., was removed. With the exception of some congestion of the lungs and one malarial attack the patient made an uneventful recovery.

Diagnosis. Dazzi used subcutaneous injections of adrenalin in 20 cases as recommended by Schittenhelm and Schlecht and independently by Neuschlosz for the diagnosis of latent malaria. He found that in doses of 1 mgm. adrenalin did not provoke a typical attack but was constantly followed by the appearance of plasmodia in the blood. They first appeared about twenty minutes after the injection, were most numerous in about an hour's time, and in another twenty-four hours all disappeared. In cases in which they were already present before the injection, their number was considerably increased. The adrenalin also caused a great diminution in the size of the spleen, except in cases of advanced sclerosis of the organ. The change in its size began a few minutes after the injection and stopped in a few hours' time.

Habetin injected 15 cases of tertian malaria which had been free of paroxysms and parasites for from three to six weeks with 0·5 gm. of sodium nucleinate in 10 c.c. of saline solution. Five cases reacted positively both as regards fever and the presence of parasites in the blood. Habetin concludes that sodium nucleinate is a suitable and harmless means of activating latent malaria, although no definite conclusions as to the extinction of the infection can be drawn from a negative result.

Prophylaxis. Paoletti found from his experiences in Albania that in spite of the administration of 40 cgm. of quinine hydrochloride daily almost all the soldiers who had this prophylactic treatment contracted malaria in the course of two months. On the other hand, no case occurred among the officers who, in addition to quinine prophylaxis, lived in mosquito-proof huts and used mosquito-nets. Paoletti does not regard quinine prophylaxis as valueless, but admits that it may be of use in malarial localities where anophelines are few and malignant forms of malaria are rare, but in districts like Albania, where malignant forms are prevalent and anophelines are present in enormous numbers, mechanical prophylaxis is the only method of value.

Treatment. Taylor, who has had more than ten years' experience of the treatment of many thousand cases of malaria in Uganda, states that a dose of calomel (gr. v) at the commencement of an attack appears to have an almost specific action in preparing the way for the quinine, and attributes to it in a very large extent the absence of complications and quick response to quinine. A saline was given the following morning and 20 grains of quinine hydrochloride in 5-grain doses were given until the temperature had become normal for twenty-four hours. The dose was then reduced to 15 grains daily for one week, then to 10 grains daily for a fortnight, and lastly to 5 grains every evening for two months. With these small doses much better results were obtained than with larger doses.

In a note on the treatment of recurrent malaria Fraser deprecates the administration of quinine in tablet form. Although tablets are pleasanter to take than quinine in solution, evasion is so much easier and so commonly practised that they should not be employed in hospital practice. Fraser states that no man can relapse when he is taking 15 grains in solution once daily. Smaller doses are not sufficient and the amount should be given in a single dose rather than in divided doses. It was not found practicable to continue the treatment beyond twenty-eight days in hospitals or in concentration camps for malaria. The interval between the completion of twenty-eight days' treatment and the occurrence of a relapse varied from several days to several weeks. The actual relapse should be treated by 15 grains of quinine sulphate in solution twice daily for four days and thereafter by 15 grains once daily.

Silvestri maintains that the only method by which a complete cure of malaria can be effected is by a mobilization of the plasmodia by various provocative methods followed by administration of quinine by mouth, which he prefers to any other method. The simplest and safest provocative method in his experience is the use of strychnin by mouth in doses of 1–3 mgm. daily, which usually causes the attack to appear within three or four days.

Stradiotti regards **intravenous injection** as superior to all other methods of administration of quinine in malaria, as it enables the exact quantity of the alkaloid to be introduced directly into the blood without dispersion of any kind. The fact that the intravenous route has been reserved for the severest cases and that it represents the most powerful method of combating the disease is a clear proof of its undoubted superiority. Moreover, from the economical standpoint it should be noted that 1 gm. of quinine injected intravenously is equivalent in its action to 3 gm. given by mouth. The difficulty of obtaining the drug in Italy, where its price has increased tenfold since the beginning of the war, should be another reason for preferring the intravenous method. The danger of gas embolism can easily be avoided by using a suitable instrument and proper technique. Certain complications such as collapse are probably due to excessive rapidity of injection of small concentrated solutions. Stradiotti recommends that the intravenous method should be employed, especially in hospital practice, even in ordinary cases, instead of being reserved as hitherto for rare cases of pernicious malaria.

Manson-Bahr points out that intravenous injection of quinine is undesirable in acute cases with cardiac involvement. Owing to the large number of parasites in the peripheral circulation the intravenous injection destroys them with great rapidity and floods the body with liberated malaria toxins which completely paralyse the cardiac mechanism.

In the treatment of cerebral malaria in Macedonia Phear obtained the best results with a solution of 10 grains of the bihydrochloride in 20 c.c. of normal saline ; 15–20 c.c. of this solution were slowly injected into a vein. The intravenous injection was supplemented by an **intramuscular injection** which by its slow absorption ensured a continued quinine effect. In a few cases large doses of quinine up to 100 or 120 grains in the twenty-four hours, given by the combined intravenous and intramuscular methods, were needed before the acute symptoms could be controlled. Although a limited amount of tissue necrosis was probably an almost constant result of intramuscular injection, it was rare to find any symptoms or signs beyond transient discomfort and a localized induration which speedily disappeared. A more serious degree of tissue necrosis, however, might occur if repeated intramuscular injections were given to patients with seriously lowered vitality, such as those suffering from the effects of chronic dysentery. A similar warning is given by Manson-Bahr, who recommends intramuscular injections of quinine for malignant malaria (12 grains in 2 c.c. of saline) early in the course of the disease. After three doses on three consecutive days there is a complete temporary disappearance of the parasites from the blood-stream, and the size and condition of the spleen rapidly become normal.

Cowan and Strong are inclined to give intramuscular injections to all cases at the outset. They regard the bihydrochloride as the most suitable drug for this purpose and inject it deeply into the gluteal muscles in doses of 10 grains dissolved in 10 c.c. of normal saline. As an exceptional measure Phear gave quinine *per rectum* in doses of 5–10 grains dissolved in 5–10 ounces of saline. The method proved of value when it was desired to supplement the amount of quinine introduced by other channels.

According to Reitler the value of **methylene blue** advocated by Ehrlich and Guttmann in the treatment of malaria has been variously estimated by different observers. Ziemann's systematic observations have shown that it has no effect. Reitler, however, was induced to use it in a number of cases owing to its good effect in a case of quartan fever which was refractory to quinine. Forty-four patients who, with the exception of the case of quartan fever, were examples of tertian malaria were treated on the day following the attack with small doses of quinine combined with 0·5 gm. of methylene blue. Reitler came to the conclusion that, though methylene blue by itself is of little or no value in the treatment of malaria, in combination with quinine or shortly after its administration it prevents any further attacks in cases of so-called resistance to quinine. It also allows the therapeutical dose of quinine to be greatly reduced, which is of considerable value in the treatment of patients who are intolerant of quinine and especially in cases of blackwater fever.

Mayer, of the Hamburg Institute for Tropical Diseases, found that methylene blue in doses of 0·2 gm. five times daily had a rapid action on the fever and the parasites in quartan malaria. Kaufmann, on the other hand, regards the use of methylene blue in malaria as only advisable when quinine for one reason or another cannot be given. In only quite mild cases can it effect a complete cure. Even in cases of well-marked quinine idiosyncrasy he thinks it advisable to combine it with small doses of other drugs, such as euquinine or Fowler's solution.

According to Rusznyák various observers have found that different substances possess a well-marked catalytic action or a high degree of toxicity in the light, while in the dark this action is either entirely absent or much less in degree. A peculiarity of these substances, to which quinine belongs, is the possession of fluorescence. Though Tappeiner and Ziemann independently found that fluorescein has no demonstrable action on the course of malaria, it occurred to Rusznyák that the effect might be reinforced by fluorescent substances. In 35 cases of malaria which had proved resistant to quinine he found that subcutaneous injections of fluorescein or eosin (0·01–0·06 gm. in saline solution) caused an immediate fall of temperature, and of 25 cases which had relapsed during treatment, 20 reacted in the same way, so that out of 60 cases only 12 failed to react. Rusznyák admits that these results must be taken with considerable reserve, partly owing to the small number of cases, and partly owing to the tendency of the febrile paroxysms, especially in chronic malaria, to cease spontaneously. The fact, however, that the subsidence of the febrile attacks so frequently coincided with the injection of the dyes induced him to publish his observations, which were moreover supported experimentally by the synergy shown *in vitro* to exist between quinine and eosin or fluorescein.

The use of **galyl** in the treatment of post-malarial anaemia is advocated by Phear and by Forbes and Lunn, the drug being given intravenously in doses of 0·4 gm. in 20 c.c. of sterile solution of sodium bicarbonate.

Pais (1) (2) has used **X-rays** in the treatment of about 290 cases of chronic malaria which were refractory to quinine, his object being to stimulate the sluggish haemopoietic organs by irradiation of the spleen. The treatment was guided by the study of the temperature. An attempt was made not to produce a sudden fall of temperature but rather a slow and stable modification of all the symptoms of the infection. The first irradiations were followed generally by a slight and transient diminution in the number of the red cells, which rapidly increased again and remained constant. The changes in the blood were accompanied by changes in the splenic enlargement. The pain in the spleen increased at first during, or a few hours after, the irradiations and the parasites sometimes appeared in the blood, but a progressive improvement of all the symptoms soon occurred and the spleen generally diminished in size. Even the largest splenic tumours yielded to this treatment. Large doses were contra-indicated, and it was necessary to proceed very slowly with small doses and with long periods of rest. The efficacy of quinine was found to be decidedly greater when it was associated with X-rays or after a series of irradiations. Small doses of the drug showed in such cases a very marked therapeutic power, while larger doses proved ineffective. In acute forms of malaria X-ray treatment was of less value.

According to Cartolari, who records six cases of **splenectomy** for malarial splenomegaly with one death, the operation is indicated whenever, by reason of excessive mobility, ptosis, fixation in an abnormal position, or torsion of its pedicle, the enlarged spleen causes the patient considerable suffering or much change in the general condition and disturbance of the various functions.

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THYROID GRAFTING

The veteran Theodore Kocher, not long before his death, made a final communication on the subject of thyroid grafting, to which his attention had been directed from 1883. He summarized his experience in a paper read to the 43rd Congress of the German Society of Surgery in April 1914. It is a subject of importance outside of goitrous countries, for thyroid medication is apt to prove insufficient, or sufficient doses cannot be borne in cases of congenital myxoedematous hypothyroidism or athyroidism, and, after excessive removal, causing cachexia strumipriva. As regards the inherent properties of cells to live and proliferate, Roux, in 1884, noted that cells of part of a cock's comb, in a warm 0·5 per cent. salt solution, underwent some development. The continuous cultivation *in vitro*, especially by Alexis Carrel in New York (*see* Hadda), of living tissue cells, by supplying the cells with a suitable artificial plasma and by providing for the removal of waste products, has demonstrated the fuller possibilities of functional transplantation. The most suggestive experiments have been autoplastic, the ingrafting of part of the animal's thyroid gland in order to protect it from the effects of the complete excision of that gland. In patients the thyroid grafting has been of the homoioplastic type, man to man, and it is towards the most efficient method of carrying this out that attention has to be directed. Heteroplastic experiments, transplantation from one species of animals to an animal of another species, also heteroplastic grafting operations, transference of an animal's thyroid gland to man, may be passed over, for the operation has at most such a transient effect as to show no advantage over thyroid medication.

Schiff, in 1884, described experiments in which the thyroid gland, a part or the whole, was transplanted *en masse* into the peritoneal cavity.

von Eiselsberg, in 1890, carried out intraperitoneal transplantations, also transplantations into the subperitoneal and subcutaneous tissues.

Kocher adopted the transplantation into the cancellous tissue of the upper part of the diaphysis of the tibia.

In 1904, Cristiani, of Geneva, introduced his multiple method of inserting small bits of thyroid gland into the subcutaneous tissue.

Carrel, in 1905, succeeded in transplanting the whole gland into the neck of the animal, and connected up the thyroid arteries and veins. The circulation through the engrafted thyroid gland might be reversed by joining the thyroid arteries of the host to the veins of the graft and *vice versa*.

In 1906, Payr, of Graz, proposed the grafting into the substance of the spleen.

Observations made upon the thyroid gland tissue after transplantation have distinguished three zones, which vary in extent according to what follows, whether the graft survives and develops, or whether its elements disappear and are replaced by the fibrous tissue of the host.

The first and most marked change begins at the centre and spreads outwards towards the periphery. After a day and a half a rapid degeneration is seen in progress, most advanced in the cells of the blood-vessels, then in the glandular elements, which lose their staining properties and disappear. The centre of the graft becomes occupied by small round cells, followed by fibrous tissue formation.

After three days there is to be noted at the periphery of a graft which is going to persist a mitosis among the nuclei of the glandular epithelium, which then proliferates. Buds are formed which grow into cylindrical collections of cells from which new alveoli develop. From the border where the tissues of the host are in contact with the graft there is seen a proliferation of the capillary endothelial cells by which new capillaries are formed, and these grow into the graft between the glandular epithelium towards the centre. An intermediary zone of variable extent comes to be occupied by small round cells after all gland tissue has disappeared. If the graft is a success, then the developing alveoli of the peripheral zone spread into it. If the graft fails, the intermediary zone changes, like the centre, into fibrous tissue, and spreads outwards. Then the newly developed alveoli in the peripheral zone in turn disappear, together with all the transplanted glandular elements.

Functional activity on the part of the graft depends at first upon the store of colloid transplanted with the original gland tissue. The newly developing alveoli do not exhibit colloid formation for some time. After three months, large alveoli are seen with columnar epithelium and containing colloid, also smaller follicles without signs of colloid formation. After six months a successful graft shows normal thyroid gland tissue. But as compared with the original size of the graft, what persists is much smaller, from one-half to one-tenth. Even six months or more after the graft has become well established, a slow process of absorption by the cells of the host may set in. The effect, however, of this late absorption may be masked by the development in the meanwhile of some previously latent thyroid gland tissue lying outside the anatomical thyroid gland.

The experiment devised by Carrel of cutting out the thyroid gland of an animal, then replacing it in position and reconnecting its blood-vessels, succeeds only because it is autoplastic, and yet may fail owing to thrombosis of the thyroid veins attended by haemorrhagic infarcts and necrosis. Homoioplastic experiments—that is, the thyroid gland transplanted into an animal of the same species—fail: the transplanted thyroid undergoes acute necrosis. Heteroplastic transplantation, the transference to an animal of a different species, fails with even greater certainty.

Experiments on the effect of transplanting small portions of the thyroid gland tissue into the middle of a lymphatic gland have resulted in the survival of autoplastic grafts for 70 days, whilst all homoioplastic and heteroplastic grafts disappear quickly, their place being soon taken by leucocytes and fibroblasts, and finally by lymphatic gland tissue.

Experiments on transplanting into the peritoneal cavity resemble those into the lymphatic glands. Even autoplastic grafts may be ultimately absorbed; homoioplastic grafts only subsist for a while. It is possible in the case of intraperitoneal transplantation to transfer half a thyroid gland along with the attached parathyroid bodies without injuring the graft in the process of transfer. Those who see in uninjured parathyroid a material more likely to persist than the rest of the thyroid gland tissue must perforce adopt this method of transplantation in man.

Payr found that as distinguished from lymphatic glands the spleen offered a more suitable tissue for a graft to establish itself. He explained this as connected with the endothelial lined spaces in the pulp of the spleen, surrounded by venules. Payr experimented by autotransplantation in cats and dogs. Half the thyroid gland of the animal was inserted into its spleen, and 10–30 days later the remaining half of the thyroid gland removed. Subsequently, in a number of the animals the whole spleen, including the graft, was excised. Of 48 experiments a complete success was reached in 8, an incomplete success in another 10. But at the best the graft only persisted from 3 months to at the longest 271 days. Too little thyrocolloid was formed. As to the objection that the spleen presents a paucity of lymphatic channels for the escape of excretory products, Payr held that colloid from the graft passed into the venules of the splenic pulp. The special point in favour of grafting into the spleen is the ready way in which the graft becomes vascularized.

Implantation into the subcutaneous tissue has been successful in the hands of Cristiani of Geneva, small bits of the thyroid gland were inserted into the subcutaneous tissue in several or many places. This multiple transplantation ensured the development of a persistent new thyroid gland tissue which lasted in cats for 4½ years after removal of the animals' thyroid glands. Bits in an uninjured state can be cut out, immediately transferred and inserted into a pocket formed in the subcutaneous tissue by a blunt method. There is then little danger of the graft being enclosed and cut off by blood-clot. As the graft becomes established there is a good chance of excreted colloid passing off by lymphatics.

The thyroid gland is the chief organ of what may be called, in comparison with the chromaffine system, the iodaffine system. It is the centre for the iodine metabolism of the body. Iodine is found in the blood nearly all in inorganic combination, only to a small amount in organic combination. It is the function of the thyroid gland to take up from the blood the inorganic compounds of iodine and to convert them into thyroglobulin.

Of this the thyroid gland holds a store which it excretes according to need.

Enderlen, in 1898, excised the whole thyroid gland from a dog's neck and transplanted it into the peritoneal cavity. Fatal tetany followed. When he transplanted half the gland at a time, tetany, if it occurred at all, was but temporary. The remaining half *in situ* maintained a sufficient excretion until the transplanted half had become adherent to the omentum or peritoneum and had restarted excretion.

The thyroid gland under the conditions which produce goitre shows a natural tendency to hyperplasia. In artificially reared trout, in which the thyroid gland is without a capsule, Marine and Lenhart described how, when goitre develops, thyroid gland tissue spreads out into muscle, fascia, and bone.

After excision of a portion of the thyroid gland the remainder exhibits, if sound, a tendency to hypertrophy, and by its functional activity to compensate for the loss.

In seeking to improve homoioplastic transplantation it is necessary to counter two factors, a natural tendency to oppose the graft as a new growth, and a mechanical opposition such as is presented by blood-clot to the graft regaining a connexion with the circulation of the host. The two aims, then, are first to diminish a natural tendency to oppose the graft, and second, to strengthen the growing force of the graft. This is not the variety of transplantation in which the graft has to serve merely as a scaffold which in time will be replaced by the tissues of the host. It is the transplantation of an organ which must not only live but become fully functional.

In case of hypothyroidism the gland fails to form sufficient thyroglobulin from iodine in the food. At a further stage of hypothyroidism the gland fails, even when supplied with iodine beyond that in the food and in a form suitable for ingestion. Under such circumstances not only is an insufficient amount of thyroglobulin excreted, but some incompletely formed thyroglobulin escapes into the circulation and acts as a toxin.

This is sufficient to show that any tendency to hypothyroidism renders a graft from such a gland unsuitable.

In the case of a normal thyroid gland, from which it is proposed to graft, a short course of iodine medication is indicated beforehand. By it the activity of the normal gland cells is stimulated and the graft will then contain a full store of thyroglobulin which will serve the recipient of the graft until such time as the graft can assume functional activity. Especially suitable material for grafts is supplied by exophthalmic and parenchymatous goitres. The cells of these growths are not only in a state of functional activity, but they possess some property belonging to new growths in general. Various experiments in relation to cancer have shown that new growths may be readily transplanted in animals, but regard must be had to opposition to the graft presented by the tissues and fluids of the recipient. Albuminous fluids of the recipient may react on the graft and produce substances deleterious to its functional activity. Ehrlich checked the growth of engrafted tumour cells by previously treating the recipient with tumour cells or with the normal tissue of the donor. Carrel and Foot in experiments on the growth of chicken-bone marrow *in vitro* found that growth was checked by adding the plasma from a rabbit previously treated with chicken-bone marrow.

There may be assumed a natural similarity between a mother and child, or other near relations, but Kocher laid stress upon the importance of examining the blood, following Abderhalden, so as to select for donor one allied in blood composition to the recipient.

Before the grafting the recipient will generally have been under thyroid treatment, and it is important that this should be continued in the most fitting way whilst the graft is taking root. Some have laid stress upon the graft including one or more of the parathyroid bodies. v. Eiselsberg in cats transplanted the thyroid gland and the parathyroids so that after 1–3 months he could remove the transplanted parathyroids, leaving the thyroid gland itself. After that tetany supervened in the cats. But on the whole, the parathyroids have been proved to be accessory, undeveloped, or latent thyroid glands. Their deep situation and the bruising entailed are an insurmountable obstacle to their use in human grafting.

In order to do the least amount of damage to the graft, the general procedure must be to expose the surface of the upper part of the lateral lobes and the isthmus. Then in a normal gland a piece may be cut out including the capsule of the gland from the upper part or apex of the lateral lobe, or an exposed lobule. In the case of a parenchymatous or exophthalmic goitre degenerating portions should be avoided. Also an encapsuled adenoma is usually unsuitable as material for a graft because it is relatively avascular and tending to myxomatous degeneration. The piece of gland cut out must be immediately transferred, this is most readily done on the small fork described by Payr, practically the same as the table fork used for taking out pickles. It should be carried out by two surgeons working simultaneously, one taking out the graft and the other preparing the patient for its insertion. If the surgeon is working singly, the graft must be kept in sterile salt solution at blood heat, but only for as short a time as possible.

Thyroid grafting is indicated if thyroid medication has been tried for six months and has failed, especially if it gives rise to exophthalmic symptoms, indigestion, &c. In addition there are patients who neglect medical treatment, so that the remaining active gland tissue they possess tends to undergo further atrophy.

Kocher's series of 93 cases is the largest under one surgeon. 56 cases answered to his questionnaire, 18 replies were flatly unfavourable, the grafts had been quickly absorbed as they are when heteroplastic animal grafts are used. 18 replies were favourable to grafting in combination with continuous thyroid medication. A marked improvement had followed and much smaller doses of the thyroidin were needed. The improvements included growth, and mental and muscular activity. 20 cases replied that after the grafting their health had been completely restored. Thyroid medication was required for only a short while, after which there was complete restoration without any need for further medical treatment. Kocher gave the history of these cases at length.

All had been homoioplastic, i. e. human grafts, except in the case of one or two patients who had objected to grafts from man. In them heteroplastic grafts from lambs had been tried, and then always into the upper part of the tibia; the relief had never lasted beyond some weeks.

Of the homoioplastic grafts, the most disappointing cases were those marked by an immediate improvement followed by relapse. An improvement hardly noticeable shortly after the operation, but which gradually sets in, proves in the end a much greater source of satisfaction.

Failure in the case of some marked cretins may be attributed to the fact that a graft from a sound and healthy man is of the nature of a heteroplastic graft in relation to the blood reactions of the cretin. This reaction may show an improvement after a course of thyroid administration, and so incidentally such a course, preliminary to grafting, may serve to distinguish cretins from other idiots, for which thyroid grafting would be out of place. As soon as there are signs of a graft becoming absorbed there should be no delay, but a second, and eventually a third or fourth grafting should be done. Kocher adopted in particular the insertion of the graft into the cancellous tissue of the upper end of the diaphysis of the tibia. He did this under a local anaesthetic, but none of the drug must come in contact with the graft. A longitudinal incision was made on the antero-internal aspect, the periosteum retracted and a hole in the tibia gouged out sufficient to hold a cherry. It is necessary to arrest haemorrhage, either by pressure for a few minutes, or by a haemostatic which is all washed away with normal saline solution. If not arrested the operation may be broken off, the cavity plugged with gauze, or tamponned by a rubber bag, or filled with a silver ball. In that case the actual grafting is done at a second operation a few days later. The excavation is washed out, then filled with warm normal saline. Into this the graft, of suitable size so as not to be compressed or bruised, is inserted by means of the fork; then over the graft the periosteum and the skin are separately sutured. The grafting can only be repeated once again in this way, viz. on the opposite side.

Payr's method of inserting a graft into the spleen is done through an oblique incision in the left hypochondrium. Forceps are thrust into the substance of the spleen on the convex aspect, the forceps dilated and the graft transferred on the fork; then sutures are inserted into the capsule of the spleen and over this the omentum is stitched. An advantage is that grafts may simultaneously be inserted into the peritoneal cavity, into the omentum, into the properitoneal tissue, or subcutaneously. If the spleen is so fixed that it cannot be drawn forward, the graft should be inserted into a fold of the omentum. Any tendency to haemorrhage is avoided by not making a free incision, and should it occur, may be checked by compressing the spleen.

Payr claimed a permanent although incomplete establishment of a functional graft. After it a child, who beforehand was an entire imbecile, learnt to stand and walk, also to speak a few words. In two years it grew 18–19 cm. in height with a corresponding increase in weight. The growth of hair, nails, and teeth made good progress, whilst the skin became normal. The child then suffered from repeated attacks of enteritis with swelling of the mesenteric lymphatic gland and spleen, also it had a spastic gait, but there was no return of the myxoedema.

Multiple subcutaneous implantation was adopted by Cristiani of Geneva, who since 1894 has made as many as 24 communications on the subject. One of his chief points is that the recipient must have some need but not too great a want. When part only of the thyroid gland has been excised from an animal, the transplanted piece undergoes active development; when the whole of the thyroid gland is removed from an animal at the time of the grafting, the transplanted piece is rapidly exhausted of its colloid and degenerates. On the other hand, there should not be too active a preliminary treatment by thyroid extract, so as to produce exophthalmic symptoms. The subcutaneous tissue of the abdominal or thoracic wall is best. A small incision is made, a track dilated with forceps, or by means of a small three-bladed dilator and the small bit pushed in on a fork. This is repeated in as many places as is wished, as many as 40 pieces have been transplanted at a time. At least one or more of the grafts survive, and have been shown to be active after years by excision of a small portion for microscopic examination. It is the method especially suitable for repetition. Cristiani has demonstrated both after experiments and after grafting in patients, that the grafts may become permanently established.

In a case of complete cachexia strumipriva, the thyroid function was practically restored by multiple subcutaneous graftings. After the first grafting the dose of thyroid extract was reduced to one-third the previous dose. Three months after the first, 38 small pieces were transplanted at a second operation. The dose was then further reduced to one-eighth; anything above this caused symptoms of hyperthyroidism. The patient married and had three children; later the dose of thyroid extract was restricted to one-tenth of that before grafting.

A child aged three with absence of the thyroid gland was grafted from a sound man aged 18. Marked physical and intellectual improvements followed, and 9 months later the transplanted pieces could be felt under the skin.

In a case in which after excision only the isthmus was left, two grafts were inserted into the subcutaneous tissue. Three years later both the grafts and the isthmus had notably enlarged. On excision of one of the grafts it was found to have increased 10 times in volume and its histological appearance was that of normal thyroid gland tissue.

In another case a graft the size of a linseed had enlarged to that of a cherry.

In the case of a woman who became pregnant after being grafted subcutaneously, it was noted that the graft swelled up during the pregnancy and subsided afterwards, just as a normal thyroid gland may do.

Klose of Frankfurt, after considering the foregoing methods, has recently recorded five cases grafted by the intraperitoneal method first introduced by Schiff. The insertion of a graft into Douglas's pouch has the advantage that a large piece can be used and implanted without setting up haemorrhage and without having to cut up the piece. The place is favourable for the vascularization of the graft, at the same time that there is ample opportunity for the absorption of colloid through the lymphatics.

Five cases were so treated: in 3 there was no improvement; in the other 2 an improvement which lasted for two years.

A piece weighing 60 grms. taken from the parenchymatous goitre of a girl was transplanted into a boy aged 13 with marked results which lasted until he was 20, when there occurred a sudden relapse. This indicated a necessity for the repetition of the grafting, and from which second grafting a more prolonged relief might be anticipated.

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SURGICAL TREATMENT OF LIVER ABSCESS

The single abscess of the liver which is amenable to surgical treatment is set up by amoebic dysentery. Under ordinary circumstances it is restricted to tropical countries and the subject is of interest chiefly to those practising in those climates.

During the war, however, surgeons who had had no previous experience in the matter were called upon to serve in countries where amoebic dysentery is endemic. Also troops from tropical countries carried amoebic dysentery to France in a larval form. There it spread in some degree to men who had never been in hot countries.

In consequence there have been some modifications and improvements in the treatment. First and foremost has been the administration of large doses of emetin, commencing in the preliminary stage of hepatic congestion. By persisting in the free administration of emetin the development of an abscess has been arrested. An early aspiration has withdrawn pus and yet there has been no occasion for further surgical treatment. The suppuration and necrosis, if not actually arrested by the emetin, is controlled. The abscess tends to remain single; there is no such destruction of liver cells or of blood so as to colour the pus.

In addition to emetin the intravenous injection of an arsenical preparation has been used, apparently with benefit.

Chauffard and Françon concluded that the administration of emetin controlled amoebic hepatitis, or if suppuration supervened, the emetin reduced it, so that only a cold abscess formed which after being laid open quickly healed. In their case emetin had served to cut short the development of the abscess. A waiter aged 25 was attacked by fever with acute pain in the right hypochondrium and shoulder. He had not been abroad, but had been in contact with coloured troops a year before. He had then acquired a typical amoebic dysentery which had recurred. Along with the general signs of acute amoebic hepatitis, there was a leucocytosis of 11,400 formed by 76·5 per cent. of polymorphonuclear cells. Ten days after the acute onset a puncture was made through the right hypochondrium without an incision, and 3 c.cm. of grumous pus removed. It contained amoebae, but was free from bacteria. There was a gradual improvement under treatment by emetin with the addition of the arsenical preparation '914', so that six weeks later the man showed a gain in weight of 3·5 kilos. Chauffard and Françon found that 10 other cases had been reported in which after pus had been withdrawn by puncture recovery followed under treatment by emetin. One case published by Mattei was examined after death from pneumonia. Before his death the signs of a hepatic abscess had subsided under emetin. There was found caseous pus enclosed in a thick walled fibrous capsule, the size of a mandarin orange.

Talbot reported 15 cases of liver abscess which he had observed in Bagdad. The signs pointing to a diagnosis which occurred in nearly all the cases were: general enlargement of the liver, fever continuous or remittent, leucocytosis with an average of 18,600 polymorphonuclear leucocytes, a local tender spot over the site of the abscess, also signs of local inflammation at the base of the right lung, with rapid wasting and severe sweating. One case died owing to the severe character of the infection and the formation of a second abscess after the first had been drained; the rest recovered.

The treatment consisted in early aspiration with the object of reducing tension in the abscess cavity; the treatment by emetin was then continued, and it was found that in two-thirds of the cases there was no occasion to proceed to drainage. Eleven cases were treated by aspiration alone. a 20 c.cm. syringe with a large needle was used and passed into the liver in various directions until the pus was found. Then without moving the needle as much pus as possible was withdrawn. It was generally yellow pus which darkened in the air, and only once was chocolate-coloured pus met with. The pus proved in some cases sterile, in others to contain the *Entamoeba histolytica*, also there were found staphylococcus, *Bacillus coli* or *Bacillus pyocyaneus* organisms in one or two cases. But the character of the organisms in the pus did not apparently matter.

Talbot considered that the majority of liver abscesses might be treated by such aspiration in combination with emetin, and that incision was needed only in exceptional cases. A drainage tube with one end in the constantly moving soft liver and the other in the more fixed chest wall appeared to him objectionable.

As regards diagnosis more importance has come to be attached to an X-ray examination; the size of the liver, a change of shadow generally in the right lobe, the position and movements of the diaphragm, materially aid in distinguishing acute hepatitis from an intrahepatic abscess, also from a subphrenic abscess or a pleural empyema, and from an abscess which has burst into the right lobe of the lung.

Upon the guidance furnished by the fluorescent screen has arisen a greater tendency to adopt surgical exploration and that at an early stage.

This has tended to supersede puncture with a trocar and cannula and the pushing the drainage tube into the abscess cavity. The more frequent adoption of surgical exploration has not been attended by undue mortality; on exposing the region of the abscess, the spread of infection has been prevented by packing around, then the finger has been gently thrust into the abscess and a drain inserted without recourse to irrigation.

Rathery and Bisch recognized in the so-called diarrhoea of the trenches a real dysentery which might lead to the quiet evolution of a localized liver abscess.

Regnault discussed the obscure signs which may precede the formation of the abscess—Anorexia, the tongue furred, the temperature irregular with a slight late-evening rise to 39° C., night sweats, a dry cough, dyspnoea, right shoulder pain, wasting, the facial aspect dull and earthy. The patient may be slightly jaundiced; it is generally difficult for him to lie on his left side, and he keeps to his back with a small turn to the right. The epigastrium and right hypochondrium become more prominent as compared with the retraction seen in cachexia from other causes, and there may be tenderness on pressure. Acute hepatitis has to be distinguished from typhoid and paratyphoid fever, malaria and cholecystitis. The acute hepatitis, if it causes dyspnoea, is difficult to distinguish from broncho-pneumonia, but that may be secondary and obscure a primary abscess. It is in such cases that an X-ray examination is important. Larval cases of hepatic abscess have been confounded with syphilis of the liver and other forms of hypertrophic cirrhosis. Suppuration in connexion with the biliary ducts or in a hydatid cyst, as also a subphrenic abscess, or an extension to the pleura, are all subjects for treatment by the same methods as an intrahepatic abscess, and therefore precise diagnosis before exploration is not of such great importance.

Regnault described the case of a lady who had lived several years in Tonkin, and whose case had baffled attempts at diagnosis, but had generally been taken to be pulmonary. She was spitting up pus, and had leucocytosis with 80 per cent. of polymorphonuclear leucocytes. An X-ray examination showed an opacity at the base of the right lung. A transpleural incision disclosed an abscess in the right lung which communicated through the diaphragm with a large abscess cavity in the liver. After drainage and a later resection of ribs to close an empyema fistula, she recovered health.

Candler's conclusions based on 13 cases were as follows. There need be no history or evidence of dysentery, and a late infection of the liver may follow long after the first intestinal invasion by the entamoeba. Fatal cases have exhibited no intestinal lesion, or there may be a small single persisting ulcer from which the hepatic suppuration is derived, probably through the capillaries of the portal vein. The suppuration in the liver shows a necrosing centre and an increasing connective tissue formation around, which destroys additional liver cells. Beyond this is a zone of hyperaemia. There is no marked leucocytosis unless pyogenic organisms complicate the amoebic infection. The pus is generally greenish yellow and slimy, not pink or brown. Amoebae are often not found in the pus first removed, but appear in that discharged by the drainage tube, presumably coming from the wall of the abscess. As for the character of the pus, Candler's cases were so insidious in onset that in half of them a diagnosis of abscess could not be made for a month. The X-ray examination was more useful in localizing a subphrenic abscess, than abscess of the liver itself, indeed an abscess might form in the liver without giving rise to a definite enlargement. For finding the abscess he put most reliance on making several punctures, using Barker's lumbar puncture needle. But these punctures might fail to discover the abscess and the signs continuing, it might be necessary to explore. Emetin was administered in doses of 1 gr. once or twice a day, but this was interrupted after 10 days for fear of a cumulative effect on the heart.

Of 13 cases, 5 were explored and drained through the epigastrium, the penetration of the liver to reach the abscess being done by blunt methods. All recovered. Seven were drained through the chest wall and diaphragm. After cutting through the diaphragm, its margins were sutured to the thoracic wall before proceeding to open the abscess. One case died on the 15th day after drainage, no progress towards repair having taken place. Besides these one case died undiagnosed. In all cases after operation the administration of emetin should be continued. Three cases of acute hepatitis subsided under emetin without going on to abscess formation.

Cope had experience of 16 cases of liver abscess in Mesopotamia. Two ruptured into the lung and recovered under treatment by emetin, 2 were aspirated and injected with quinine hydrochloride and these also recovered, as did likewise 10 submitted to free drainage together with the administration of emetin. There were 2 deaths among the 16, one from multiple abscesses and one from secondary infection through the drainage tube, owing to the treatment after operation being forced to be conducted in a dirty hut.

The concurrent administration of emetin is not mentioned by some. Thus Gibson saw 5 late cases: 3 were single and successfully drained, 2 cases had multiple abscesses and died after drainage had been set going. J. G. Jones saw 4 cases in Bombay, all fatal after operation because the abscesses were multiple.

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W. G. S.

COLEY'S TREATMENT OF SARCOMA OF THE LONG BONES

The conservative treatment of sarcoma of the long bones carried out by Dr. W. B. Coley of New York has attained a measure of success in his hands. He has produced evidence that by its means the lives of some patients suffering from periosteal sarcoma have been indefinitely prolonged. Also his method offers an alternative to amputation. If in the hands of others Coley's treatment has not met with like success, the details of his procedure which he gave in June 1919 may serve to show that he has been more thoroughgoing than his imitators.

Butlin in 1900 furnished some carefully prepared statistics, which were fully confirmed by the speakers in the debate on the subject at the Royal Society of Medicine in 1913. The only difference was that the primary mortality after amputation had become a negligible quantity. But the results of amputation at the earliest possible stage for periosteal sarcoma confirmed Butlin's statement that it failed absolutely to cure. Indeed, it remains doubtful whether the amputations actually prolonged life in many of the cases. Most of the recent cases have died after amputation from metastases and not from recurrence in the stump. Even if one conjectures that some instances were not truly metastases, but fresh outbreaks of sarcoma, such a view tells in favour of Coley's treatment. A boy aged 7 had a rapidly growing sarcoma of the upper part of the left radius. After due examination, the arm was amputated at the shoulder-joint and the axillary glands removed. Four years later, he returned with a sarcoma of the outer orbital angle of the right frontal bone. This was followed by further sarcomatous growths, appearing at first to be clinically discrete and then fusing with one another. He was some months under observation before there was a diffusion of the sarcoma wide enough to cause death.

The contrast between periosteal and central sarcoma, the structure of which exhibits multinuclear giant cells, and the cures achieved by amputation, or more simply by erasion, has led to a proposal to change the usual name from myeloid sarcoma to myeloma. It is intended by the latter term to express the idea that it is a benign new growth. This is an exaggeration of the stage to which actual knowledge has reached. Neither clinically nor histologically can a sharp line of distinction be drawn between the tumour which is truly local and one which kills ultimately by metastasis. There are undoubted differences; the central sarcoma of the upper end of the tibia or of the lower end of the radius is generally more benign than that of the femur or humerus or innominate bone. Histologically a relatively small number of giant cells has been held to indicate a benign growth; others have found distinctions in the stroma between the giant cells. As a matter of fact central cystic tumours may be inflammatory in origin, having started as chronic staphylococcal or tuberculous osteomyelitis, and giant multinucleated cells are found in the soft lining of the cysts. It is often difficult to distinguish such a case, especially when complicated by haemorrhage from a myeloid sarcoma undergoing cystic degeneration. Platou of Christiania under the term osteitis fibrosa would seem to include an intermediary category, occurring not only in young people, but also at ages between 50 and 60. Osseous cysts arise either after fracture, or a slighter injury. Rheumatic pain may be followed by bending or spontaneous fracture. The cavities of such cysts may contain a brownish red or yellowish fibrous tissue with few cells; in others the fibrous tissue contains numerous large giant cells. Such cases are amenable to erasion. But Platou did not really describe any definite points to prove that he was not referring to a slow-growing type of myeloid sarcoma attended by fibrocystic degeneration and new bone formation. The danger to the patient is that his life may be cut short by a late metastasis, having the structure of myeloid sarcoma.

Coley in a paper read at a meeting of the American Surgical Association on June 16, 1919 referred to cases which he had observed within the preceding five years. He had in December 1916 related to the Southern Surgical Association 200 cases of sarcoma of the long bones, since then he had observed an additional 50 cases.

One of the earliest signs, especially of periosteal sarcoma, is deep and boring pain, hence time is misspent on treatment for rheumatism before the tumour is discovered, whether by palpation or by X-ray examination. The pain has its origin in the deeper layers of the periosteum, whence it spreads outwards into the surrounding dense fascia. An early exploration is most important and a piece should be removed for histological examination, notwithstanding any hypothetical objection as to a risk of starting metastasis. A conservative line of treatment had been advocated by others for myeloid sarcoma, but not all giant-celled sarcomas are benign. Thus of 40 cases diagnosed as giant-celled sarcoma, 8 died of metastases; a myelogenous mixed giant-celled sarcoma of the lower end of the femur may be regarded as malignant, that of the upper end of the tibia as relatively benign.

O. Kocher of Tübingen in 1906 described 33 consecutive cases of central myelogenous sarcoma, of which, however, the microscopical examination was incomplete. Four were too advanced for amputation and ended fatally. Eleven were amputated, 1 died of the amputation, 8 of metastases, 2 were known to be alive over two years and 1 was lost sight of.

Periosteal sarcoma of the long bones is regarded by every one as very malignant and the diagnosis by means of a microscopical examination presents no difficulties. Coley formerly practised amputation, but he had found that lives might be saved by treatment with his preparation of mixed toxins, even in cases in which amputation had been declined. In some cases radium appeared to be of assistance, but in others not. In one case of periosteal sarcoma of the femur, toxins were administered for a month and failed, then radium was applied, and the growth apparently disappeared for two years. After that period it recurred, and massive applications of radium had no influence, so amputation was done, but death followed in a few months from pulmonary and spinal metastases. One large and rapidly growing chondrosarcoma of the upper part of the humerus was treated by introducing radium tubes and applying radium emanations externally. The tumour disappeared, but a sinus persisted where the radium tubes had been introduced. Scrapings from the sinus showed degenerated sarcoma cells but no active ones.

In another case the upper part of the tibia was occupied by a giant-celled sarcoma to the extent of 5 inches. Treatment by curetting, toxins and radium was followed by almost complete restoration of the destroyed bone and the patient was well nearly 4 years afterwards. Even a case inoperable by amputation at the hip-joint had apparently been cured.

In the previous 5 years Coley had treated 60 cases of sarcoma of long bones.

Femur 32; humerus 14; tibia 9; fibula 3; clavicle 2.

Of the 32 femur cases, 13 were amputated after the conservative treatment had failed, 11 were still living and 2 had died of recurrence of the sarcoma.

Four refused amputation. Of these

(1) A large central sarcoma of the lower end of the femur was treated by toxins and radium; later death occurred from metastases in the lungs.

(2) A central sarcoma of the lower end of the femur extended into the knee-joint, and, after treatment by toxins only, was well 5 years later.

(3) A sarcoma of the lower end of the femur involving the knee-joint and upper end of the tibia was treated by toxins and radium. The case was well three years later and walking without support (see a fuller note below).

(4) A large inoperable sarcoma of the upper half of the femur was treated by toxins and radium and was well, without any sign of recurrence, two years later.

Among the cases amputated were: a case of periosteal sarcoma of the femur treated first by toxins followed by amputation, which continued well for 3 years, then there was recurrence and death. Two cases after treatment by toxins were amputated and had continued well for 6 months; three cases were amputated and then treated by toxins, two continued well for three years and then one recurred, and one died of recurrence nearly three years after the amputation. The following cases were described more fully.

(1) A female aged 21 who had noticed the disease for 8 months was found on exploration to have a central sarcoma of the lower end of the femur which had penetrated into the knee-joint, and which proved on microscopic examination to be a vascular giant-celled sarcoma. Amputation was declined. The mixed toxins of erysipelas and *Bacillus prodigiosus* were then administered, beginning with 1 minim dose and increasing by ½ minims up to 8½ minims, when the temperature rose to 104° F. After a week, the treatment was resumed and continued for a year, 73 injections in all. The exploratory incision suppurated, later a counter-opening was necessary in the popliteal space, after which healing occurred. The treatment was begun in November 1914; the case was exhibited in November 1916, January 1919, and at the meeting in June 1919. She was wearing an apparatus to fix the knee and had 2½ inches of shortening, but walked without a crutch or stick.

(2) A woman aged 29 had noted the swelling for 7 months. It involved the lower end of the femur and had extended to the knee-joint and upper end of the tibia. Amputation was refused. On exploration a giant-celled sarcoma was found which was curetted away under the control of a tourniquet, leaving a cavity the size of an orange which was packed. The treatment by toxins was continued up to a dose of 14 minims; there was no reaction until 10–12 minims were reached. In the course of two months, the cavity filled up, the X-rays showing progressive ossification. Then radium was inserted through the sinus and radium emanations applied externally. The treatment was begun in November 1915, and she was exhibited in October 1919 walking with a crutch and without recurrence.

(3) A man aged 39 had, three weeks before, noted a swelling of the lower third of the left leg. On exploration a small spindle-celled periosteal sarcoma was found to involve the lower third of both tibia and fibula. The toxin treatment was begun in April 1917, a temperature of 102–104° F. being provoked 4–5 times a week. In May radium emanations were applied in addition. The treatment was interrupted from July to September when enlargements were found in the femoral, inguinal, and iliac glands, the largest the size of a hickory nut. A gland was removed and found to be invaded by an actively growing large polyhedral-celled sarcoma. Radium emanations were applied to the groin from September to December 1917 and the toxins continued for two years with short interruptions. He was exhibited in June 1919, i.e. after $2\frac{1}{2}$ years of treatment, when there was no sign of the primary growth nor of any metastases.

(4) A man aged 36 fell on ice and fractured the left femur a little below the trochanter. There had been no sign of a tumour beforehand, nor did the X-ray examination immediately after the accident show anything pathological, but 9 weeks later an increasing swelling at the site of the fracture was noted. This happened in January 1917 and in the following October Coley found an inoperable sarcoma. Severe reactions were produced by toxins and radium emanations were also used. The active treatment was continued until June 1918, when it was intermitted. In October 1918, there was no sign of a primary tumour, bone had disappeared, a false joint had formed, and a Thomas's splint was used. He was exhibited in October 1919, i.e. two years after the commencement of the treatment. There was then no sign of a primary growth nor of metastases.

(5) A man aged 29 had noted pain in the lower end of the left radius for 5 months. A central myeloid sarcoma of the lower end of the radius had involved the bone for 3 inches and had caused a pathological fracture; the ulna and soft parts were involved but not the skin. In April 1918 the injection of $\frac{1}{8}$ minim of the toxin into the growth caused a severe reaction, T. 104° F., nausea and vomiting, also marked herpes on the lip, but a subcutaneous injection did not set up a reaction until 6 minims were reached. There was no improvement until the toxins were given every other day in sufficient doses to produce a T. 102–104° F. By July 1918 the swelling had entirely disappeared. Injections three times a week were continued until January 1919 when he was able to recommence work as a grocer, with the wrist fixed in a case. He was exhibited in October 1919, i.e. 18 months after the commencement of the treatment, when there was no sign of recurrence. New bone formation had nearly united the pathological fracture.

The treatment failed to control the following very malignant case.

(6) A man aged 20 whilst wrestling sprained his leg just below the knee. Slight pain and lameness persisted, and after 8 weeks a swelling was noted. Ten weeks after the accident the limb was explored and a periosteal large round-celled sarcoma was found to involve the fibula from its head for $5\frac{1}{4}$ inches downwards. The tumour quickly invaded the knee-joint and the patient soon lost 20 lb. in weight. Toxins were administered and produced slight chills, radium tubes were introduced through the drainage tube sinus and radium emanations were applied. Besides involving the knee the tumour quickly fungated out of the sinus. Amputation was then done and the toxin treatment continued. Metastases appeared in the chest 4 months after the amputation and death followed 2 months later.

53 cases of periosteal sarcoma of the humerus had come under observa-

tion of which only two were known to have survived over three years; in one case this was attributable to the toxins.

A man aged 35 sustained a spiral fracture of the middle of the shaft of the humerus. Two weeks later a swelling was noted which proved to be due to the growth of a periosteal round and spindle celled sarcoma. The swelling disappeared under treatment by toxins, but recurred 6 months later, when amputation at the shoulder-joint was done. The sarcoma then removed had the appearance of a highly malignant spindle and round celled sarcoma. The growth recurred in the pectoral muscle, but disappeared after prolonged toxin treatment. The patient was alive without further recurrence 8 years later.

Between 1890 and 1919 Coley observed 250 cases of sarcoma of long bones, of which 35 were alive and well over 3 years. The disease recurred after 3 years in 5 cases, 1 tibia after 7 years, 1 ulna after 7 years, 1 femur after 5 years, 1 tibia after 5 years, 1 femur after 5 years.

	Total observed.	Alive and well over 3 years.	
		Periosteal.	Central.
Femur	114	9	7
Humerus	53	1	1
Tibia	40	2	5
Fibula	9		
Radius	12	2	3
Ulna	8	2	
Clavicle	11	2	
Metacarpal	2		
Metatarsal	1	1	
	250	19	16

A toxin combined with radium treatment without amputation was adopted in 17cases, 6 periosteal and 12 central. Of these 12 remained well over 3 years.

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W. G. S.

THE RELATIONSHIP BETWEEN TENDON REFLEXES AND MUSCLE TONE

The long controversy as to whether the tendon phenomena are due to direct stimulation of the appropriate muscles or are true reflexes has finally been settled in favour of their reflex origin. With this conclusion has come the acceptance of the knee-jerk—being the most widely employed of the tendon-jerks—as a direct indicator of the degree of muscle tone. It appears to be generally assumed that in both cases the reflex arc concerned is the same.

Although it is still widely held, both clinical and experimental observers have always recognized that there are certain difficulties in accepting this view completely. On the one hand, neurologists find that in cerebellar disease a brisk knee-jerk may co-exist with profound and widespread muscular hypotonus, while Sherrington records that after spinal transection in such an animal as the cat, when the activity of the postural reflex is low; that is, when muscle tone is at a minimum, the knee-jerk may be just as readily obtainable and as brisk as in the tonic decerebrate animal.

Very commonly, on the other hand, the degree of muscle tone and the facility of the tendon reflexes do run parallel. In peripheral nerve disease and in such an affection of the afferent path as tabes dorsalis we find hypotonus and diminished or absent tendon-jerks; while in those conditions of disease of the nervous system in which muscle tone is heightened and there is true hypertonus, the tendon reflexes are also notably increased in amplitude and facility.

These varying relationships between tone and tendon reflexes are not so conflicting as appears at first sight, and the factors underlying them may be expressed as follows: interference with the integrity of the appropriate spinal reflex arc impairs or abolishes both muscle tone and tendon-jerk: impairment of cerebral control over the activity of the arc from disease involving the pyramidal system of neurons results in increased muscle tone and tendon-jerks: certain nervous lesions of prespinal level, such as may be seen in disease of the cerebellar system, interrupt, or at least throw out of gear, the reflex arc concerned in the maintenance of the postural reflex, of which muscle tone is the expression, but they do not necessarily interfere with the activity of the tendon reflexes. In short, loss of muscle tone is only associated with tendon arreflexia when the former is due to a lesion of the spinal reflex arc, commonly on the afferent side. Hypotonus from defective activity of higher level arcs need not be associated with loss of tendon reflexes.

Sherrington speaks of the knee-jerk as a true proprioceptive reflex, and he finds that when it is elicited in the spinal animal soon after transection of the cord it is readily obtainable and ample. Its graphic record in these circumstances shows that the relaxation of the muscle is rapid and complete and is often followed by a few to and fro oscillations due partly to the inertia of the flaccid limb. In the decerebrate animal where reflex tonus is high, the knee-jerk, though not more facilely obtained than in the spinal animal, shows in its graphic record a feature not found in the reflex of the former. The relaxation phase reveals a definite and maintained shortening of the contracting muscle, which may endure for several seconds. This is the 'shortening reaction', which Sherrington has found to be characteristic of the muscle whose postural tonus is high, and it is, therefore, this element of the knee-jerk which affords an indication of the degree of muscle tone present, rather than the initial jerk contraction. He concludes 'that the knee-jerk which is now on good grounds to be regarded as a true reflex, should commonly be brisk or exaggerated in those conditions in which the postural action or "tonus" of the extensor muscle is also well marked or exaggerated, may probably be because certain of those same reflex arcs which execute the one also execute the other. But the knee-jerk itself is not a postural reaction, and is therefore not a direct sign of tonus. And the central connexions normally involved in the postural reactions of the muscle are more extensive than those required for mere exhibition of the jerk. This would explain the fact often commented upon that the briskness or amplitude of the jerk does not always go hand in hand with hypertonicity.'

This conclusion has received striking confirmation in the observations of Gordon Holmes and of Riddoch. Thus Gordon Holmes's graphic records of the knee-jerk in cases both of recent and of long-standing cerebellar injury show the same rapid and complete relaxation and the pendulum-like oscillations that Sherrington has described. In normal individuals Holmes found that the relaxation was less rapid than the initial contraction, and he says 'evidently then a tonic contraction, or state of tone, in the extensor muscles prevents the immediate fall of the normal leg to the abscissa'. Similar observations had been made previously by André-Thomas and these are referred to in Holmes's paper.

Entirely in accord with these findings and of even wider import are Riddoch's observations on the occurrence and character of the knee-jerk in spinal man. In these circumstances, the phase of flaccid paraplegia and tendon arreflexia originally described by Bastian, and now known to be analogous with the 'spinal shock' described in animals by Sherrington, may under favourable circumstances give place to a second phase; one of intense spinal reflex activity. This includes among its phenomena a return of the knee- and ankle-jerks. Riddoch states that 'a very important feature of the extensor tendon-jerks in spinal man is the quick falling away of the contraction. The quadriceps muscle responds briskly to the sharp tap on its tendon, but it immediately relaxes again and the leg drops like a dead weight. There is no tonic prolongation of the contraction such as occurs in the intact individual . . . . . .'

In spinal man, then, the knee-jerk has the characters it has been found to possess when it occurs in a toneless muscle; it consists of a rapid jerk contraction with an equally rapid and complete relaxation. It is evident, therefore, that in the normal individual the knee-jerk possesses two elements; the initial jerk contraction and the 'shortening reaction' secondarily induced by it in a muscle endowed with reflex tone. This second element is the expression of the activity of those arcs which are common both to reflex tone and to the tendon reflex, and is the only element of the normal jerk from which we may rightly draw conclusions as to the state of muscle tone present in a given instance. This is hardly a decision within the scope of ordinary clinical methods.

That the knee-jerk may be brisk and ample after spinal transection indicates that the jerk element has a reflex arc of spinal level. Muscle tone, on the other hand, has its reflex centres at prespinal level, and it may even include the cerebellum among these. It is true that after spinal transection in animals there may be fleeting and inconstant manifestations of postural tone. Probably, as Sherrington suggests, such spinal centres as the reflex employs are kept up to the mark for that reaction by influences exerted on them by prespinal centres under normal conditions. It certainly appears from Sherrington's researches that as we ascend the animal scale the spinal component of muscle tone becomes progressively more subordinate to the prespinal and of less importance. Whether it has any physiological value in spinal man is at least doubtful, and Riddoch's observations on the knee-jerk point to this view. It is, therefore, the more unexpected to find Riddoch stating that in spinal man 'the reappearance of the extensor tendon-jerks is dependent on the return of tonus in the vasti cruris and calf muscles'. This hardly accords with his observation that in these circumstances the knee-jerk obtained is such as is characteristically found in a toneless muscle and lacks the 'shortening reaction' indicative of the presence of reflex tone.

This discrepancy may find an explanation in the unsatisfactory nature of the clinical test he employs to estimate tone. The need of a good quantitative clinical test for tone has long been felt, and the value of palpation of a given muscle between finger and thumb is recognized as very small: indeed, the method is positively misleading. As Kinnier Wilson has pointed out (*Brain*, 1912, **34**, 470), it is a common observation that when we lift the rigid leg of a hemiplegic from the bed, the calf may be found pendulous and soft to touch. Its hypertonus, which may be extreme, can be estimated only by passively stretching the calf muscles by dorsiflexion of the foot. When we attempt this we find almost at once that the range of passive movement is limited by the development of an active resistance on the part of the muscle. The same is found when we stretch the knee extensors by flexing the limb at the knee, though the vasti may be very soft to palpation. A further confusing factor is that in spinal man during the phase of reflex activity, passive manipulations of the legs readily induce reflex spasms which must give rise to possibilities of error in a simple palpation test for tone. It seems, therefore, that the last quoted observation of Riddoch's will not bear analysis, and is probably the expression of a passing reversion to the old loose sense of the word 'tonus', as it was commonly employed before Sherrington had defined the scope and purpose of reflex tone, and not as it is used elsewhere in Riddoch's valuable contribution to our knowledge of spinal function in man.

In conclusion, it may be stated that since both muscle tone and tendon-jerk are proprioceptive reflexes arising in the muscles concerned, any interference with the peripheral afferent neurone must impair the activity of both arcs and correspondingly depress both tone and tendon-jerk. On the other hand, interference with the cortico-spinal path; that is, a pyramidal tract lesion, releases both arcs from cerebral control and produces concurrent increase of both tone and tendon-jerk.

In the intact individual the knee-jerk is modified by the presence of reflex tone in the muscle subserving it, but it can be obtained with equal facility in the toneless muscle, though lacking the tonic prolongation or 'shortening reaction' seen in the former circumstances. The reflex arc of muscle tone is much more complex than that of the simple jerk contraction, and hence a lesion of the nervous system involving it and leaving intact the spinal arc of the jerk, such for example, as a lesion of the cerebellum, or a spinal transection above the level of the lumbar cord, gives us the paradoxical combination of hypotonic muscle and brisk tendon-jerk.

Boeke and others, largely from histological investigations, have concluded that voluntary muscle has a double innervation, cerebrospinal and sympathetic, and that the phasic and tonic forms of activity and the two components of the knee-jerk may be specially related to one or other element of this double nerve supply. A discussion of these hypotheses is beyond the limits of the present review, but the question will be reviewed by Dr. E. D. Adrian in a forthcoming number of *Medical Science*.

Finally, it may be suggested that clinical observation does not entirely confirm Sherrington's view that the tendon-jerk is a reaction characteristic of extensor muscles; that is, of muscles normally possessing postural tonus. In man certainly, tendon-jerks are obtainable from muscles of both flexor and extensor groups with equal facility. It is true that the tendon reflexes commonly employed in the lower limbs in clinical investigations: namely, the knee- and ankle-jerks, are both extensor jerks, but Walshe has drawn attention to the presence of reflexes from the hamstring muscles (hamstring-jerks) which follow the general laws found to obtain for other tendon-jerks. He found, also, that in 'paraplegia in flexion', when the reflex activity of the extensor group of muscles is minimal or in abeyance and the knee- and ankle-jerks may be absent, that the hamstring-jerks persist with unimpaired facility.

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F. M. R. W.

ABSTRACTS

SURGERY

Crowther, C. La sutura completa primitiva nelle ferite penetranti del ginocchio [**Primary suture in penetrating wounds of the knee-joint.**] *Arch. ital. di chir.*, 1919, **1**, 215.

Crowther gives details of all the cases of penetrating wound of the knee-joint, 31 in all, treated by him by the method of primary suture. 25 of these were under observation from beginning to end. All were associated with severe injury of the articular surfaces. In 8 the patella alone was injured, in 8 the femur alone, in 4 the tibia alone, in 2 both tibia and femur, in 2 femur and patella, in 1 tibia and patella, in 1 femur, tibia, and patella. The projectile was a grenade fragment in 13 cases, a fragment of shrapnel in 10, a bullet with explosive effect in 2, a fragment of stone in 1. In 12 cases the projectile was retained; in 11 of these the fragment, either free in the joint or embedded in the tibia or femur, was extracted: in 1 case the fragment, which had traversed the joint, was not discovered and gave rise to no subsequent complications. In 16 cases the wound of the knee was accompanied with other injuries; in 2 it was bilateral, and in 1 the circulation was seriously interfered with. The immediate results of the operation were: in 24 cases, 22 cures by primary union, 1 severe suppuration of the joint necessitating secondary amputation, and 1 death on the seventh day from gas gangrene which developed in a fracture of the femur of the opposite limb, the injured knee remaining free from infection and healing by first intention. Of the 5 cases not included in the above the details were lost owing to a sudden retreat; the cases were, however, under observation for two weeks, and appeared to have healed by first intention without complications. Crowther attributes these successful results mainly to the rigorous asepsis maintained during the performance of the operations, and considers that the unsatisfactory results obtained by some surgeons were due to shortcomings in this matter.

Crowther limited himself as far as possible to a linear longitudinal incision carried through the aperture of entry of the projectile; in the majority of cases this was sufficient. If it did not permit of a complete exploration a contralateral opening was made, or the patellar tendon cut through by an L- or U-shaped incision. After removal of the projectile and any loose fragments, and excision of contused tissues, the joint cavity was abundantly and repeatedly irrigated with sulphuric ether and the capsule closed with catgut suture.

Crowther operated within ten hours of wounding, on the average, excluding one case from the calculation, in which the operation was delayed for eighty hours. The favourable results were probably in part due to this early intervention, but the author considers that many surgeons attach too great an importance to this point. The nature of the lesion appears to have greater influence on the result. If the lesions are limited to the synovial membrane and foreign bodies are not retained in the joint cavity the period for justifiable operation is relatively long and may extend almost up to the moment of appearance of inflammatory symptoms. If, on the other hand, there are osseous lesions or retention of fragments in the joint cavity, and particularly of fragments of clothing, the time available is greatly reduced.

There are only three contra-indications to the operation: definite evidence of the existence of infection, complete destruction of the articular end of the femur or tibia, and extensive destruction of the soft parts. In all other cases the operation is practicable. T. W. P. L.

Niosi, F. Nuovo contributo alla conoscenza del volvolo dello stomaco. [**Volvulus of the stomach.**] *Arch. ital. di chir.*, 1919, **1**, 275.

Case I. The patient, a woman aged 41, had at the age of 15 a severe attack of pain in the upper part of the abdomen. This came on suddenly after a meal and lasted half an hour. The pain was situated mainly in the left hypochondrium and was accompanied with a twisting sensation and frequent efforts at vomiting resulting in the expulsion of merely a small quantity of acid liquid. A similar attack occurred three years later, and again on the day preceding operation. In this last attack, which came on after an abundant meal, in addition to the symptoms mentioned, there were distension of the abdomen and a dragging sensation in the neck. The patient drank a small quantity of liquid, which, however, did not give the sensation of having reached the stomach, and was regurgitated four hours later, when ineffectual efforts at vomiting commenced. The abdomen was enormously distended, especially in its upper two-thirds; there was no visible peristalsis. In the epigastrium and left hypochondrium a firm, smooth mass of about the size of the hand could be felt. Neither spleen nor stomach could be delimited by percussion. The pulse was 120–130. A diagnosis of perforated gastric ulcer was made and laparotomy performed. The firm body felt on palpation proved to be the spleen, considerably enlarged, intensely congested, and displaced forward; it was twisted on its axis so that the inferior margin was uppermost. Above and to the left of the spleen was the transverse colon, lying immediately beneath the diaphragm: the stomach was hidden by the mesocolon. The small omentum, ecchymosed and partly lacerated, was twisted into the form of a cord. Stomach, colon, and spleen were then taken in the two hands and turned in the direction of the hands of a watch through about 400°. The first half-turn brought the spleen and colon back into their normal positions, but the volvulus of the stomach was not completely reduced, and the pyloric portion lay in front of the fundus. In the production of the volvulus the pyloric portion appears to have followed the anterior abdominal wall, revolving from right to left, while the cardiac portion underwent an inverse movement forward and to the right. The second half-turn brought the pylorus back into its normal position. After reduction the duodenum and pylorus showed great motility owing to the elongation of the small omentum, and the stomach was enormously distended. There was no stenosis of the pylorus. Posterior gastro-enterostomy was performed and the anterior surface of the stomach sutured to the abdominal wall. The patient made a good recovery and was seen repeatedly after the operation, in perfect health.

Case II. The patient, a woman aged 42, began to suffer, twelve years previously, from pains in the left hypochondrium radiating to the epigastrium and back. The pains had no relation to meals and lasted from half to one hour. On the day before coming under observation, an attack of unusual severity occurred, accompanied with vomiting and abdominal distension; the vomited matter consisted at first of a colourless mucoid liquid, but later became dark and foetid. The abdomen was enormously distended in its upper half, the distension being ovoidal in form, diminishing from right to left and from above down, with a well-defined limit immediately below the level of the umbilicus. The lower half of the abdomen was flat, contrasting markedly with the distended upper portion. There was no visible peristalsis. The spleen could be felt below the costal margin, but the splenic area was not increased. A diagnosis of volvulus of the stomach was made, and a sound passed with the intention of evacuating the stomach contents. No obstruction was met with at the cardia and about two litres of brown liquid were withdrawn. The abdominal distension completely disappeared and there was complete relief from pain, vomiting, and other symptoms. Six days later a bismuth meal was given and an X-ray examination revealed an hour-glass constriction at about the middle of the stomach. Laparotomy was performed and the constriction found to measure about 8 cm. in length and three finger-breadths transversely. The pyloric division presented a certain degree of torsion, the greater curvature being directed forward. An ample anastomosis was made between the pyloric and cardiac sacs, and posterior gastro-enterostomy performed. Examined some months later the patient appeared to be completely cured.

T. W. P. L.

Leotta, N. L'ulcera semplice della porzione digiuno-ileale dell' intestino tenue. [**Simple ulcer of the jejunum and ileum.**] *Arch. ital. di chir.*, 1920, **1**, 349.

Simple ulcer of the jejunum and ileum has been recorded twenty-one times only; but inasmuch as all the cases came under observation in consequence of perforation, it is probable that they are of more frequent occurrence than these records suggest. The patients have usually appeared to be in perfect health at the time of the attack, although in individual cases conditions have been present which might have a causal relation to the disease, such as acute infection, gout, diabetes, lead poisoning, dyspepsia, and abdominal injury. In more than half the cases the ulcer was situated near the lower end of the ileum; but any part of the bowel may be affected. In three cases the ulcers were multiple. In one case only did the ulcer show thickening of the edge and base indicative of chronicity.

Leotta's patient was a healthy man of 25, who was suddenly seized, on the day following excess in eating, with violent pain in the right iliac fossa. The pain rapidly became diffused over the whole abdomen and was followed by vomiting and diarrhoea. Examined on the third day the patient had all the symptoms of general peritonitis. Laparatomy was performed and a perforated ulcer of the ileum found at about 20 cm. from the caecum. The ulcer was of the size of a cent piece, situated on the free border of the bowel, round and sharply punched out. As far as could be ascertained the rest of the bowel was normal. Widal's reaction was negative. Microscopically the ulcer had all the characters of a simple acute ulcer originating in a circumscribed necrotic patch of mucous membrane, similar to that met with in the stomach. The edge was composed of a narrow zone of necrosed tissue, and inflammatory exudate was slight, except on the peritoneal surface.

T. W. P. L.

NEUROLOGY

Kramer, S. P. On contralateral representation in the cerebral cortex of the peripheral blood-vessels. *Contributions to Medical and Biological Research,* dedicated to Sir William Osler, 1919, **2**, 857.

In a previously recorded case of cortical tumour, Kramer noticed that while removing the growth the crossed radial pulse became perceptibly weaker and remained so for some hours after both first and second stages of the removal. He has since observed a similar phenomenon in two cases of gunshot wound of the cortex, the difference amounting to as much as 20 mm. of mercury.

In a series of observations on dogs, Kramer found that stimulation of the leg area of the motor cortex causes a general fall of blood-pressure, and in addition a localized fall in the opposite leg. This he determined by dividing the femoral artery on both sides and measuring the pressure directly. By alternate stimulation of the two leg areas, crossed alternating depression of the blood-pressure was registered in the femoral arteries. The fall in pressure appears to be due to a local dilatation of the vessels of the crossed limb.

F. M. R. W.

Holmes, Gordon. Pain of central origin. *Contributions to Medical and Biological Research,* dedicated to Sir William Osler, 1919, **1**, 235.

The rarity with which lesions in the central nervous system cause pain, compared with the relative frequency with which injury and disease of peripheral nerves do so, has naturally given rise to a belief that central nervous lesions are painless unless they also involve the meninges or the peripheral sensory structures.

However, within recent years, clinical investigation has revealed that lesions affecting certain of the central nervous organs may give rise to peripherally referred pain. In the case of the thalamus we have the best-known example of this. Déjerine and Roussy first described the 'syndrome thalamique', in which from disease affecting the lateral and posterior parts of this organ there results persistent or paroxysmal pain, often of great severity, referred to the affected half of the body or to some part of this. An over-reaction to affective stimuli is a characteristic feature of this syndrome.

Head and Holmes, working together, have concluded that these pains and this excessive uncontrolled reaction to certain forms of peripheral stimulus depend not upon an irritative lesion of central conducting paths, but upon the removal of the control normally exerted over the thalamus by the cerebral cortex.

Pain of medullary origin is very rare, but during the war Holmes observed a few cases of spinal injury in which pain could not be ascribed to root irritation. This was seen in cases of concussion with or without slight direct injury of the cervical enlargement of the cord.

In these the pain is intense and burning in character. It is never strictly radicular in distribution, but more diffuse, spreading down the arms and over the shoulders and part of the chest. Though generally constant, these pains are increased by peripheral stimuli, particularly by movement of the painful parts. While they endure they are of intolerable severity, and commonly overcome the patient's fortitude. Fortunately they seldom last for more than three or four days before they begin to abate in severity, to cease in about three weeks. Holmes discusses the reasons which have led him to believe that sensory root irritation cannot account for these symptoms, and one of the more decisive of these is that the pains are sometimes remote from the level of the lesion. Of the 16 cases examined, in 12 there was a partial Brown-Sequard syndrome, in the remaining 4 the symptoms were of moderate severity and bilateral.

In the unilateral cases it was found that the *pain* was on the same side as the paralysis, and not crossed as was the *loss* of pain and thermal sensibility. From which Holmes concludes that the anatomical changes underlying the pain must be in the ventro-lateral columns of the side of the cord opposite to the paralysis, where the afferent impressions excited by the stimuli of pain, temperature, and touch are conveyed after their decussation from the side upon which they enter the cord.

On investigating sensation on the paralysed side, which was the seat of the pains, he found that there was 'hyperaesthesia' to touch, pressure, pricking, heat, and cold. All these forms of stimulus gave rise to great discomfort and even to bouts of pain. Further, the threshold of stimulation to these forms of sensibility was not raised in many instances. Therefore the lesion of the crossed sensory paths cannot have been so severe as to interrupt conduction, and the pains may be due to the irritative effects of a slight lesion of these conducting paths.

From the fact that painful sensations may be produced by so wide a variety of stimuli, Holmes suggests that when nerve fibres are injured pain may not be exclusively due to impressions conveyed by the normal pain-conducting paths. Stimulation of any form, if it be of sufficient intensity or mass, may be summated so as to acquire an intensity capable of eliciting actual suffering.

Like the pains and hypersensitiveness of the thalamic syndrome, which they greatly resemble, these of medullary origin may be accompanied by sensations of exaggerated pleasureableness when stimuli endowed with pleasureable feeling tone are employed. F. M. R. W.

Clauss, M. Über Polyneuritis im Kindesalter. [**Polyneuritis in infancy.**] *Deutsche Ztschr. f. Nervenh.*, 1920, **65**, 169.

Clauss remarks on the rarity, apart from postdiphtheritic neuritis, of polyneuritis in children. Only forty cases are on record. He adds six personally observed examples. Of these, three were of quite unknown aetiology, one was associated with an acute rheumatic polyarthritis, one followed whooping cough, while the third was associated with various tuberculous manifestations. F. M. R. W.

SCHOB, F. Hemichorea und Hemiathetose nach Schädeltrauma. [**Hemichorea and hemiathetosis following a skull injury.**] *Deutsche Ztschr. f. Nervenh.*, 1920, **65**, 210.

Hemichorea and hemiathetosis are rare sequels of skull wounds. Schob has been able to find but two cases recorded during the period of the present war, while v. Monakow has collected the few pre-war examples in his '*Gehirnpathologie*' (S. 538).

Schob's case was that of a sailor, who seven years before coming under observation had received a severe fracture of the right parietal region of the skull from a revolving anchor capstan. At the time the right half of the vertex was severely damaged and the underlying brain contused. There was left hemiplegia with periodical epileptiform fits. With the gradual recession of the paralysis, involuntary movements appeared in the limbs of the left half of the body. Clinical examination showed that these involuntary movements contained three elements (1) rapid jerky choreiform movements involving arm, leg, and face; (2) slower, sinuous, writhing movements of athetotic form in hand and hallux; (3) a more or less continuous mobile spasm of the arm and foot. There were in addition, signs of a moderate degree of impaired function of the pyramidal tract on the left side; that is, hemiparesis with the usual reflex alterations. There was also hemianaesthesia.

It was noted that operation, the trimming off of irregular bony fragments, and the evacuation of a cyst, resulted in marked diminution of the choreiform movements, but not of the athetosis, while during his fits, the same dissociation was found, the chorea ceasing, while the athetosis persisted. F. M. R. W.

PATHOLOGY AND BACTERIOLOGY

JONES, HORRY. Some factors influencing the final hydrogen-ion concentration in bacterial cultures with special reference to streptococci. *J. Infect. Dis.*, 1920, **26**, 160.

This work was undertaken to determine if successive transfers of a given organism in the same medium, inoculated under the same conditions would develop an identical hydrogen-ion concentration. This was found to be the case with *S. haemolyticus*, *B. typhosus*, *B. paratyphosus*, and *B. proteus*.

Next, the author studies the effect of temperature, initial reaction, and composition of medium in causing deviations from that final hydrogen-ion concentration. For details of these latter effects the paper should be consulted. W. A. M. S.

LEGROUX, R. Succédané du liquide d'ascite pour quelques cultures bactériennes. [**Substitute for ascitic fluid as a culture medium for bacteria.**] *Compt. rend. Soc. de biol.*, 1920, **83**, 466.

Owing to the difficulty of obtaining ascitic fluid in large quantities, especially for meningococcic diagnoses, the author recommends the use of serum which contains a small quantity of formalin. One c.c. of commercial formalin is added to 600 c.c. of ox or horse serum which need not be sterile.

After shaking, 1,200 c.c. of distilled water are added, and the medium is then tubed and sterilized in the autoclave at 112°–115° C. For the final medium 1 c.c. of the formalinized serum is added to 7 or 8 c.c. of bouillon. This medium is capable of replacing ascitic fluid for most bacteria with the exception of gonococcus. W. B.

Otteraaen, A. Haemolytic streptococci in the throat in certain acute infectious diseases. *J. Infect. Dis.*, 1920. **26**, 23.

The author examined the throat, mouth, and nose, of 300 patients suffering from acute infectious diseases for haemolytic streptococci. In the mouth 11 per cent. were positive, in the throat 60 per cent., and in the nose 16·3 per cent. Of the 300 patients, 130 had diphtheria, of whom 58 (46·6 per cent.) gave positive cultures; 125 had scarlet fever, of whom 98 (78·4 per cent.) gave haemolytic streptococci. The remaining 45 had miscellaneous diseases with 20 (44·4 per cent.) positive cultures. In a series of 35 normal persons the author found haemolytic streptococci in 57 per cent., while in another series of 33 normal persons, the percentage of positive results was 21·2. Tables are given containing the results of other investigators. In the author's experience the cultures were not very virulent for animals. Fermentation tests showed that according to Holman's classification the strains fell into the pyogenes and anginosus groups. The author recommends a preliminary enrichment in serum broth, glucose blood broth, or cooked meat before plating. W. B.

Clawson, B. J. Varieties of streptococci with special reference to constancy. *J. Infect. Dis.*, 1920, **26**, 93.

This is a laborious study of a large series of cultures of streptococci, especially with reference to morphology, fermentation reactions, haemolysin production, and immune reactions. In the series of 134 haemolytic strains, the haemolytic property was constant after nearly two years cultivation on artificial media. Haemolytic streptococci were found in 37 per cent. of 200 normal throats, and may occur in horse faeces, milk, and occasionally in human faeces. Only 4 of the 134 haemolytic cocci failed to ferment lactose within 5 days: only 2 always fermented mannitol, and only 3 always failed to ferment salicin. From the author's experiments it appears that there is more uniformity of fermentation among haemolytic than among non-haemolytic streptococci. He considers that none of the minor groups of haemolytic streptococci show sufficient relation to source, habits, or pathogenesis to warrant a separate classification. Of 150 strains of cocci which did not produce haemolysis, 5 always failed to ferment lactose, 36 always fermented mannitol, and 75 always fermented salicin. The author considers it doubtful whether any of the sub-groups of non-haemolytic streptococci really deserve a place in classification. Agglutination reactions between haemolytic cocci and homologous serum in the author's series showed a high degree of uniformity. The reactions of 'haemolytic' serum with non-haemolytic cocci, 'non-haemolytic' serum with haemolytic cocci or 'non-haemolytic' serum with non-haemolytic cocci, except with homologous strains, gave a low percentage of positive results. The same in general is true of the complement fixation tests, thus strengthening the belief that the haemolytic streptococci constitute a more homogeneous group than those which do not produce a haemolysin. The research was carried out in the department of Hygiene and Bacteriology of the University of Chicago.

W. B.

Davis, D. J. The fate of *Streptococcus haemolyticus* in the gastro-intestinal canal. *J. Infect. Dis.*, 1920, **26**, 171.

According to the author haemolytic streptococci are found in the throat in a large number of persons, and must therefore frequently be swallowed. Their subsequent fate is the subject of the present communication, the experiments having been carried out in rabbits. Haemolytic streptococci do not occur normally in any quantity in normal rabbits, and when introduced into the stomach in large quantities only occasionally pass through the canal to be found in the faeces. Examination of the alimentary canal at different levels indicates that they neither develop appreciably nor are able to establish a footing. The gastric juice of normal acidity from man or rabbits kills haemolytic streptococci in from 2 to 5 minutes. Gastric juice in achylia may not kill them for several hours. In normal human faeces haemolytic streptococci were not found in 53 cases. Haemolytic streptococci mixed with normal faeces will live at the temperature of the ice chest for at least several days, but rapidly die out in the incubator at 37° C. W. B.

Gay, F. P. and Stone, R. L. Experimental streptococcus empyema: attempts at prevention and therapy by means of vaccines and serum. *J. Infect. Dis.*, 1920, **26**, 265.

The work detailed in this paper was carried out with one strain of streptococcus isolated from a fatal case of streptococcal empyema in a human subject. This strain was grown on media containing 1 per cent. glucose in one series of experiments, and 5 per cent. fresh rabbit serum in another series. No difference in the antigenic property of the organisms grown on these two media have been found.

Experimental empyema in rabbits was produced by injecting measured quantities of this culture into the pleural cavity. The empyema produced resembled closely the empyema in a human subject, except that it was not found possible to produce the accompanying broncho-pneumonia. The empyema produced was invariably fatal, the average time to cause death being 5 days.

Experiments to obtain localization in the pleural cavity by intravenous injection of the cultures were without positive results. Experiments were carried out to test the possibility of protecting rabbits against the formation of an empyema by previous inoculation with killed cultures, with killed followed by living cultures, and with living cultures only. It was found that an appreciable degree of immunity could only be produced by prolonged inoculation extending over many weeks, and carried out with both killed and living cultures.

The serum from animals which have been immunized successfully by these injections has been tested and found to contain specific agglutinins, opsonins, and precipitins in a high degree. This serum has been used in attempts to prevent or cure experimental empyemata in rabbits. Intravenous and intrapleural injections were tried. The number of animals tested was small, but a small percentage of successes are claimed.

Attempts were made to influence the course of an experimental empyema by subsequent inoculation with killed cultures, but without success.

G. T. W.

de Kruif, P. H. and **Ireland, P. M. Streptolysin.** *J. Infect. Dis.*, 1920, **26**, 285.

This work has been carried out mainly with the haemolysin of the beta type of haemolytic streptococcus, and is largely of a quantitative character. The authors used the supernatant fluids of cultures which had been centrifugalized a high rate. Although not sterile, such fluids contain trivial numbers of cocci, and yield very consistent results. The minimal haemolytic dose of the lysin was taken as that quantity of the supernatant fluid, of a culture, which produced complete haemolysis of 0·5 c.c. of a 2·5 per cent. suspension of three times washed sheep's red corpuscles at the end of 2 hours at 37° C. Serum bouillon was the culture medium employed. On such a medium streptolysin is rapidly formed, and may reach a maximum in 7 to 8 hours. The results of bacterial counts made at the same time as the haemolytic tests showed that the flow of streptolysin occurred during the early part of the logarithmic growth period of the culture. At the end of this time the free lysin begins to disappear rapidly, and may have completely disappeared in 14 hours. A comparison of the persistence of the lysin in whole cultures of streptococci and in the supernatant fluids of centrifugalized cultures, showed that lysin might still be elicited from the former, although they had completely disappeared from the latter. The authors consider that this is due to residual lysin operating from the surfaces of the cocci. The comparative efficiency of sheep, horse, human, and rabbit serum bouillon was studied, sheep and horse serum being found superior to human, and greatly so to rabbit serum. In general heated serum was better than unheated. All sera, active or inactive, rose sharply from comparatively low titres in 5 per cent. concentration to high values, the maximum streptolysin production being reached with 20 per cent. concentrations of horse, sheep, and human sera, and 25 per cent. of rabbit serum. On the basis of these results the authors recommend a blood plate which will yield a maximal streptolysin production. Sheep blood is defibrinated and centrifuged, the serum being removed and heated to 56° C for 45 minutes. The heated serum is recombined with the red cells in the proportion of 4 parts of serum to 1 part of cells. One part of the serum-cell mixture is then added to 3 parts of a 1·5 per cent. liquid agar which has been melted and cooled to 45° C. The final concentrations of this medium are serum 20 per cent., red corpuscles 5 per cent., and agar 75 per cent.

W. B.

Savage, W. G. Cats and human diphtheria. *J. Hyg.*, 1920, **18**, 448.

It has been a common belief for some years, especially in this country, that cats may suffer from diphtheria, and that they not uncommonly convey the disease to human beings. Savage, in his interesting paper, has analysed all the available data, and concludes that this view is entirely without foundation. It is true that cats can be infected with diphtheria bacilli injected into them, or they may die from inoculation of diphtheria toxin. Normal cats may also harbour in their throats bacilli which present a striking morphological resemblance to Loeffler's bacilli as has been demonstrated by the author, but the occurrence of a definite diphtheria naturally, among cats, is not proved. In four instances personally investigated by the author, only one showed an organism which might possibly have been a non-pathogenic diphtheria bacillus. In the other three organisms resembling the diphtheria bacillus morphologically turned out on cultivation not to be that micro-organism. Although massive doses of living cultures were applied to the throats of kittens, it was found impossible to infect them, although, injected subcutaneously, two of the cultures killed kittens. Feeding experiments were also ineffective, as were intranasal applications. The secretion from the mucous membranes of cats appears to be particularly unfavourable or inimical to the establishment of true diphtheria bacilli. W. B.

Small, J. C. and **Dickson, G. K. Grouping of *Bacillus influenzae* by specific agglutination.** *J. Infect. Dis.*, 1920, **26**, 230.

By agglutination and absorption tests the authors believe that it is possible to separate four types of influenza bacilli. The total number of cultures examined by them was ten. W. B.

Baatz, —. Zur Frage der Auflösung von Tuberkelbazillen durch spezifische Immunstoffe. [**On the question of the lysis of tubercle bacilli by specific immune substances.**] *Centralbl. f. Bakteriol.* (&c.), I. Abt. Orig. 1920, **84**, 81.

In 1912 Kraus and Hofer published the results of experiments which led them to the view that, in the peritoneal cavity of guinea-pigs previously rendered tuberculous, tubercle bacilli become altered tinctorially and morphologically in a manner resembling the granulation of cholera vibrios in the classical publications of R. Pfeiffer. Kraus and Hofer also stated that the serum of tuberculous guinea-pigs possesses greater power than normal serum in bringing about a lysis of tubercle bacilli. The present author, working in Pfeiffer's Institute, has repeated Kraus and Hofer's experiments, but has failed to obtain any evidence of bacteriolysis of the tubercle bacillus.

W. B.

McCoy, G. W. and **Bengtson, Ida. Notes on the detection of *B. tetani*.** *Bull. No. 115, Hyg. Lab.*, Wash., 7.

This investigation was carried out to throw light on the occurrence of a number of cases of tetanus following vaccination against small-pox. The material examined consisted of 'ivory' points, 'sterilized' and unsterilized, glycerinated vaccine virus in bulk, on points, and in capillary tubes, and glycerinated vaccine used for propagating the virus. The material was cultivated in fermentation tubes or in Kjeldahl flasks with an oil covering, and in a number of instances animal inoculations were carried out. Unsterilized 'ivory' points to the number of 10,966, were examined, and tetanus bacilli were found 7 times. Of sterilized uncharged points there were 8,568, and 4 showed tetanus. Cut off charged points to the number of 5,377, were examined and revealed tetanus 4 times, none being found in the other material examined. Other questions investigated were (1) the effects of heating to different temperatures on growth of tetanus spores, (2) comparison of heating to 70° C, and no heating on the growth of spores, (3) the effect of other spore-bearing microbes on the development of tetanus spores. The tetanus cultures were isolated by diluting the inoculum, and subsequent heating of the inoculated deep agar shakes to 70° C. W. B.

Foulerton, A. G. R. The protozoal parasites of the rat with special reference to the rat as a natural reservoir of *Spirochaeta ictero-haemorrhagiae*. *J. Path. & Bacteriol.*, 1919, **23**, 78.

This is a good critical analysis of the recent work on rat trypanosomiasis, rat-bite fever, spirochaetal jaundice and spirochaetal seven-day fever, and embodies the author's own observations on the occurrence of the parasites of these various diseases among English, especially London, rats. Thus, of 123 rats examined for trypanosomes, 43 were found to carry *T. lewisi.* Six examinations of London rats for *S. morsus muris* were made, but with negative results. Of 101 rats examined (viz. 3 *Mus rattus* and 98 *Mus decumanus*) *Spirochaeta ictero-haemorrhagiae* was found in 4 of the latter species by inoculation into guinea-pigs. One of the strains was passed successively through 25 guinea-pigs. W. B.

Sierakowski, S. Ueber die Einwirkung verschiedener Methoden der Impfstoffbereitung auf den Agglutinationstiter der gegen Cholera und Typhus Schutzgeimpften. [**The manner in which different methods of preparing bacterial vaccines behave as judged by determinations of the agglutinating titre of the serum of persons inoculated against cholera and typhoid.**] *Centralbl. f. Bakteriol.* (&c.), I. Abt., Orig. 1920, **84**, 161.

This contains the results of observations on the agglutinating titre of the sera of human beings inoculated with typhoid or cholera vaccine which had been prepared by different methods such as heat, formalin, phenol, glycerine, chloroform or ether. Although chloroform and formalin sterilization was found satisfactory for the preparation of typhoid vaccine, they were unsatisfactory for cholera vaccine. Sterilization by heat alone without the addition of an antiseptic subsequently is unsafe on account of the possibility of contaminations. Agglutination after a second injection of cholera vaccine was found not to be higher than after the primary injection, and in any case the agglutinins had disappeared from the blood in six months. Sensitized typhoid vaccine is not worse than unsensitized. W. B.

Spray, R. S. Observations on paratyphoid bacilli recently isolated from animals. *J. Infect. Dis.*, 1920, **26**, 340.

An extensive investigation, briefly reported, of strains of paratyphoid-group bacilli isolated from the intestines of swine during an outbreak of infective enteritis. These were compared with strains from hog cholera. Thirty-four out of forty strains studied in detail were typical *B. suipestifer.* Two were identical with *B. paratyphosus A,* and two with human *B. paratyphosus B.* Two were intermediates. *B. enteritidis* was not found.

W. B.

Twiss, Edith M. The effect of pasteurizing temperatures on the paratyphoid group. *J. Infect. Dis.*, 1920, **26**, 165.

The authoress has made a study of the results obtained when cultures of *B. typhosus*, *B. paratyphosus A* and *B*, *B. enteritidis* and *B. suipestifer* in milk are subjected to 'pasteurizing' temperatures. Negative tests of comparatively small samples removed during pasteurization or just at its close, cannot be taken as indicating that all the bacteria are killed, for when infected milk which had been heated to 60° C., kept there for a definite time and then cooled, was incubated at 37·5° C. pathogenic bacteria were recovered after exposures exceeding those of practical pasteurization. Thus *B. paratyphosus B* was recovered from milk which had been heated to 65° C. for 30 minutes. The other bacteria behaved in like manner. There was evidence that just before the exposure that was lethal to all the bacteria, there is a period of survival which is irregular, some more resistant individuals surviving the destructive temperature. W. B.

Oppenheim, C. J. The human faecal streptococci. *J. Infect. Dis.*, 1920, **26**, 115.

This is a study of 323 strains of streptococci isolated from 55 stools of 15 perfectly normal adult persons, and constitutes an important addition to our knowledge of this important subject, especially in connexion with the supposed aetiological significance of streptococci in sporadic or epidemic diarrhoea. The author finds that mannitol fermenting non-haemolytic cultures are the predominant streptococci of the faeces of normal human beings, haemolytic cultures being exceptional. A classification of the non-haemolytic cocci found by the author gave the following results according to the nomenclature of Holman; *Streptococcus faecalis* 73·0 per cent., *S. salivarius* 1·0 per cent., *S. non-haemolyticus* i, 23·0 per cent., *S. equinus* 1·5 per cent., and *S. ignavus* 1·5 per cent. Examination of the diarrhoeal stools from specific (typhoid) and non-specific diarrhoeas as well as after catharsis suggested that the streptococci found were not such marked mannitol fermenters as those of normal persons. Indeed the fermentation of carbohydrates was in general less active. Stools from infants conform to the types found in adults although slightly less frequent numerically. The paper is prefaced by a good account of the work of other observers on the subject. W. B.

McLeod, J. W. and Ritchie, A. G. The serum reaction in bacillary dysentery. Observations on agglutination with special reference to the use of freshly prepared bacillary emulsions. *J. Path. & Bacteriol.*, 1920. **23**. 217.

This paper deals with the determinations of the agglutinating titres of the sera of three groups of human beings, viz. (1) those from whose stools dysentery bacilli have been isolated, (2) those who were presumably normal, and (3) those who had had an illness possibly dysenteric, but from whose stools dysentery bacilli had not been recovered. The Oxford technique in general was followed. but in place of standard emulsions the authors used fresh emulsions which they believe to be more specific in that they react well with the sera of infected persons, and but little with those of normal individuals. It is to be regretted that the exact technique of the preparation of the emulsions (whether bouillon or agar, formalinized or not) is not stated. In Group I there were 47 men from whose stools strains of Flexner-Y bacilli had been isolated. Eighty-three per cent. had sera agglutinating Flexner or Y bacilli to a titre of 1 : 40 or over. Among the 38 cases represented by the 83 per cent., 20 had sera with a titre above 1 : 40 for both Flexner and Y. In 6 the titre was higher for Y than for Flexner. Of these 6, 4 were the subject of Y infections and 2 with strains agglutinating equally to Flexner and Y sera. Two alone of the 20 had sera agglutinating Flexner much better than Y emulsions, and both these two were infected with bacilli which agglutinated equally with Flexner and Y sera. Only 3 of the 46 patients had sera which showed any co-agglutination of Shiga suspensions, and then even it was slight (1:10–1:20). With regard to Group II, which comprised 583 presumably normal persons, two sub-divisions were made. Of 100 hospital patients giving no history of dysentery 70 showed no agglutination, 15 had sera agglutinating Flexner and Y-emulsions below 1:20, and 15 had sera with a titre of 1:12–1:30, two only reaching the higher figure. The remainder of this group comprised 438 American infantrymen who had just arrived in France. 377 showed no agglutination with their sera, or none beyond 1:12 dilution. The sera of 61 others had a titre of 1:12–1:35. Two persons in this group who gave higher titres were found to have been the subject of dysentery and were therefore excluded from the group. These figures are very much lower than the determinations made by Rajchman, Western and T. R. Ritchie on medical students in London and undergraduates in Cambridge, and those made by Glynn and his co-workers in Liverpool. The difference in technique may have been the explanation of the diversity.

With reference to Group III there were 194 persons, of whom 25 or 12·8 per cent. yielded sera with a titre over 1:40, and had been, according to the authors, presumably infected with dysentery at some time. This figure, added to the average percentage of cases in which dysentery bacilli were actually found, gave a total of 45 per cent. of proved bacillary dysenteries passing through the army dysentery centres in France. The examination of a number of 'inagglutinable dysentery strains' led the authors to conclude that atypical strains did not play any important part in the dysenteries of the army in N. France. W. B.

Berridge, E. M. and **Glynn, E.** **Observations on the classification of forty-eight strains of Flexner-Y and allied bacilli mainly by serological tests.** *J. Path. & Bacteriol.*, 1920, **23**, 199.

This is a detailed analysis of 48 strains of Flexner-Y dysentery bacilli examined mainly by absorption tests to determine to what extent certain diagnostic dysentery sera in general use corresponded to the different types isolated. Thirty-one of the forty-eight cultures were made the subject of special analysis, and according to agglutination and absorption tests were shown to fall into six subgroups corresponding to the grouping of the War Office Dysentery Committee. The diagnostic value of the Oxford-Y sera was greater than that of the Lister-Y. Grouping by absorption was more definite than by agglutination alone. A variable amount of agglutinin common to the group occurred in all the sera. No correlation was disclosed between the serological subgroups and their fermentative activities in maltose, dextrin, salicin, and sorbitol, except that the Flexner subgroup showed a greater tendency to ferment saccharose. Certain culturally 'atypical dysentery bacilli', specially selected because they exhibited a moderate degree of agglutination with Flexner serum, could not be distinguished serologically when absorbed with only one Flexner-Y serum, but only by absorption with several. Typical Flexner-Y cultures rarely showed acid agglutination, whereas cultures which were atypical almost invariably did so. W. B.

Benians, T. H. C. A record of an inagglutinable form of Shiga's dysentery bacillus experimentally derived from an agglutinable culture. *J. Path. & Bacteriol.*, 1920, **23**, 171.

An inagglutinable strain of Shiga's bacillus was recovered from the second puncture of an abscess caused by the inoculation of a guinea-pig with an agglutinable Shiga's bacillus emulsified in a 5 per cent. mucilage of tragacanth. From the first puncture of the local infiltration, one month after the inoculation, the bacillus was still agglutinable. The inagglutinable strain was isolated one month later and was associated with colonies of typical Shiga. From subcultures of the inagglutinable strain colonies were obtained both of typical agglutinable and inagglutinable bacilli. Even the inagglutinable colonies were of two types on agar, viz. clear and opaque. They failed to absorb agglutinin from a standard Shiga serum, and also to produce an agglutinating serum in rabbits. The agglutinable strain produced from the inagglutinable entirely absorbed the agglutinins from a standard serum, and was also agglutinogenic. Both strains produced congestion of the large intestine, the inagglutinable being lethal in 3 days to rabbits after an intravenous inoculation of 1 c.c. of a seven-day-old bouillon culture. Rabbits immunized by either strain were protected against a lethal dose of the homologous as well as the heterologous culture. No agglutinins were observed in the serum of the animal injected with the inagglutinable culture, but the latter was more readily destroyed by the bactericidal serum substances than the agglutinable race. The original guinea-pig showed neither agglutinating nor bactericidal properties in its serum. W. B.

Stewart, M. J., Vining, C. W., and **Bibby, J. P. Subacute yellow atrophy of the liver in a case of syphilis following treatment with galyl.** *J. Path. & Bacteriol.*. 1919, **23**, 120.

This is a short account of the autopsy findings on a girl, aged 21, who died one hour after a slight operation, for venereal warts, performed under a general anaesthetic. Four months previously she had been treated for secondary syphilis with a course of four injections of 0·45 grm. each of galyl. Some mercury had also been given by the mouth. A fortnight after the last dose of galyl, and ten weeks before death there had been slight jaundice lasting only two days. The autopsy disclosed a liver weighing 39 oz. and presented typical red and yellow atrophy, the latter greatly predominating. The red areas showed almost complete destruction and absorption of the hepatic cells, whereas the yellow areas showed well-marked fatty changes but no necrosis. The authors consider that the initial hepatic lesion (represented by the red wasted areas) was probably the direct result of the four injections of galyl, and the patient was well on the road to recovery when the administration of ether produced such an effect on the damaged organ that death immediately ensued. The thymus gland was large and fleshy and weighed 17 grm., and the Malpighian bodies of the spleen were unusually prominent. W. B.

Sierakowski, S. Ueber Mitagglutination bei Cholera. Beitrag zur Diagnose der Cholera. [**On co-agglutination in cholera. A contribution to cholera diagnosis.**] *Centralbl. f. Bakteriol.* (&c.), I. Abt., Orig. 1920, **84**, 178.

The author studied, by agglutination and absorption tests with cholera serum, a series of seven vibrios isolated mostly from the Vistula. One of the cultures, however, came from a cholera convalescent. Six of the strains did not liquefy gelatin and four did not produce indol. All were only slightly virulent for guinea-pigs. None were haemolytic. In all cases the colonies were like cholera but less transparent. After cultivation for nearly two years one of the indol formers lost this power and the only gelatin liquefier also lost its ability to liquefy. All, however, retained their agglutinability. With a horse serum that agglutinated genuine cholera vibrios to a titre of 1 : 51,000, the vibrios isolated gave titres from 1 : 1.600 to 1 : 51,000. With a rabbit agglutinating serum which clumped cholera in a titre of 1 : 6,400 two of the strains agglutinated in a dilution of 1 : 1,600 and four were not agglutinated at all. In complement fixation tests only one of the vibrios (from water) agreed with *V. cholerae.* None of the cultures gave Pfeiffer's reaction, and true cholera was not agglutinated by sera obtained from the water vibrios, which were divisible into three groups antigenically.

In absorption tests with cholera serum the vibrios were not able to withdraw the agglutinins for *V. cholerae,* and the author concluded that the vibrios, however like cholera, were not true cholera vibrios. He emphasizes the importance of the absorption test and the existence of co-agglutination in the diagnosis of cholera. The exact technique by which the emulsions were prepared for the agglutination tests is not stated. W. B.

PRAUSNITZ, CARL. Weil-Felix Reaktion und X 19 Immunserumagglutination. [**The Weil-Felix reaction and its relation to immune serum agglutination by X 19.**] *Centralbl. f. Bakteriol.* (&c.), I. Abt., Orig. 1920, **84**, 103.

It is known through the observations of Weil and Felix, Csépai, Braun and Salomon, and others that the X 19 agglutinins in the sera of typhus patients is destroyed at 56° C., whereas the agglutinins in the sera of rabbits immunized with Proteus X 19 are thermostable. Werner and Leoneanu injected twelve persons in Roumania with killed cultures of X 19 and obtained similar results. As the experiment was done in a thoroughly typhus-stricken region the question of a previous typhus infection in these inoculated people could not be excluded with certainty. The present author, who was not exposed to typhus, inoculated himself with cultures of Proteus X 19 and then tested his serum for agglutinins. He found that the agglutinins were thermostable, as occurs in the rabbit, and he considers that this serves to differentiate the thermolabile (Weil-Felix) reaction from the thermostable Proteus immune serum agglutination. The true Weil-Felix reaction cannot, he thinks, be interpreted as the immediate result of a Proteus X 19 reaction. W. B.

WEIL, E. Ueber die Bewertung der Agglutinationsreaktionen bei Fleckfieber mit verschiedenen Mikroorganismen. [**On the value of agglutination reactions on different micro-organisms by typhus serum.**] *Deutsche med. Wchnschr.,* 1920, **46**, 343.

This is mainly a polemical article combating the view of da Rocha Lima that the serum of typhus patients acts not only on the Proteus X series but also on other bacteria. W. B.

Otto, R. and **Papamarku, P.** Weitere Beiträge zur experimentellen Fleckfieberinfektion des Meerschweinchens. [**Further contributions to experimental typhus infection in guinea-pigs.**] *Centralbl. f. Bakteriol.* (&c.), I. Abt., Orig. 1920, **84**, 12.

Report on the results of inoculation of a series of guinea-pigs with material containing the unknown virus of typhus fever. The source of the virus in these experiments was the blood of a patient in Wilna, 2 c.c. being injected intraperitoneally. The disease was afterwards propagated by passage, the most suitable inoculum being brain emulsion containing the virus. Of 114 animals inoculated intraperitonally or subcutaneously only two (1·75 per cent.) showed no symptoms. W. B.

McIntosh, J. and **Turnbull, H. M. The experimental transmission of encephalitis lethargica to a monkey.** *Brit. J. Exper. Path.*, 1920, **1**, 89.

This paper describes the apparent reproduction of human encephalitis lethargica in a monkey by inoculation of a filtered emulsion of brain. Dr. McIntosh, employing a similar technique, had previously inoculated without success into Macaque monkeys and rabbits portions of the central nervous system obtained from more than eight fatal cases. The material for the present experiments was obtained from a girl, aged 17 years, who died in a virulent, isolated epidemic of encephalitis lethargica in a home for girls at Derby. Dr. MacNalty, who investigated the epidemic, forwarded the brain and brain-stem in 33 per cent. glycerine. A summary is given of Dr. MacNalty's description of this most interesting epidemic.

A fortnight after the arrival of the brain, portions of the cervical cord and pons were removed for histological examination. No evidence of inflammation was found in these segments. Portions of the cervical cord, pons, and basal ganglia were washed, and emulsified in sterile saline for inoculation experiments. Of the emulsion, unfiltered, $\frac{3}{4}$ c.c. were inoculated into the cranium and 5 c.c. into the peritoneum of a Macacus monkey. On the thirteenth day after inoculation the animal became drowsy and weak. The weakness increased, and on the twentieth day the animal was killed. At necropsy, tuberculous broncho-pneumonia was found. Microscopic sections were made of the mid-brain, pons, and cervical cord. Apart from a few small haemorrhages in the mid-brain, no changes of significance were discovered. Of the emulsion, filtered through a Berkefeld filter, 1 c.c. was inoculated in the cranium and 5 c.c. into the peritoneum of a Patas monkey. On the sixth day after inoculation the animal had a fit. From this it had completely recovered on the following day. On the forty-eighth day after inoculation it had a severe fit in which it lay rigid and dazed. From this it recovered somewhat, but considerable rigidity and trembling, associated with lethargy, continued until death on the fifty-sixth day.

Naked eye and microscopic examination revealed no lesions in the viscera. An extensive microscopic examination of the central nervous system is given in detail. In addition to engorgement, hyaline thrombosis, a very few haemorrhages into 'perivascular canals', oedema of certain cranial nuclei, and extensive degeneration of bodies of neurons, an inflammatory infiltration was found. This infiltration affected, and was most conspicuous in, the posterior part of the left basal ganglia and the junction of the left basal ganglia with the mid-brain; it was also present in focal areas of the cerebral pia and in the wall of a vessel in the right trapezoid body. In its strict localization, its situation, its distribution in the affected areas, and in its cytology it resembled closely the infiltration in human cases.

Other monkeys were inoculated and reinoculated with emulsions of the basal ganglia and cord of this Patas monkey. In one reinoculated monkey symptoms have developed.

The paper is illustrated by drawings of the infiltrations in the Patas monkey and in a human case. H. M. T.

Moore, Hiram D. Complementary and opsonic functions in their relation to immunity. A study of the serum of guinea-pigs naturally deficient in complement. *J. Immunol.*, 1920, **4**, 425.

It is well-known in complement fixation tests that the fresh serum of certain guinea-pigs is very deficient in complement and cannot be employed. The present author refers to unpublished work by the late R. C. Downing, who found that as much as 1 c.c. of fresh guinea-pig serum might produce no haemolysis of sensitized corpuscles, and further, that in breeding experiments it was found that complement deficiency is a heritable condition. In the present research Moore utilized a large number of these complement-deficient animals and tested their power of laking sensitized blood corpuscles, as well as their powers of resistance and production of antibodies towards bacterial infections of *B. cholerae suis*. It was found that the lack of complement in the serum was not due to the presence of anything interfering with the action of the amboceptor. The lack of complement was not inimical to the establishment of an acquired immunity, for, in animals possessing the defect, repeated inoculations gave positive evidence of both bacteriolytic and agglutinating substances, and were resistant to living cultures just as were ordinary guinea-pigs whose sera were rich in complement. With regard, however, to inoculations of *B. cholerae suis* in non-immunized animals there seemed to be a significant difference in the two classes, for out of 100 complement-deficient guinea-pigs 77 died after the injection of living bacteria, whereas only 20 succumbed of 100 normal complement-containing guinea-pigs. The author points out that death was not necessarily to be attributed to the lack of complement, as it is possible that the complement-lacking animals may have been defective in other unknown ways. The author also made a number of opsonic determinations in the two classes of guinea-pigs, using typhoid bacteria and, as phagocytic agent, the leucocytes of the horse. A distinctly subnormal opsonic power was found in the sera of all the complement-deficient guinea-pigs in comparison with normal ones. The complement titre varied with the opsonic index and in the same direction, and the author believes that complement and opsonin bear a definite relation to each other.

W. B.

Kolmer, J. A. The nature of thermolabile haemolysins. *J. Immunol.*, 1920, **4**, 403.

This paper deals especially with experiments which were made to determine the relation of the natural haemolysins in human serum to human complement, and of anti-sheep immune haemolysins in rabbit serum to rabbit complement, as it has been alleged that natural haemolysins may be of the nature of differentiated complements. This view arose on account of the fact that the natural anti-sheep haemolysins in human sera are, in part at any rate, thermolabile, being destroyed or inactivated at 56° C. for 30 minutes. Kolmer finds from his experiments that the natural haemolysins in human serum are more resistant to heat than complement, and that there is no relation between the complement content and the natural haemolysins in human sera. Absorption of active human sera with corpuscles removes haemolysin but not complement. Filtration may remove complement leaving behind the whole or a large part of the lysin. W. B.

Kolmer, J. A. The influence of desiccation upon natural haemolysins and haemagglutinins in human sera. *J. Immunol.*, 1920, **4**, 393.

This paper contains the records of experiments which were made to determine the influence of desiccation upon human natural haemagglutinins and natural haemolysins. The titres of the sera were carefully determined in the liquid state and then the sera were dried by distributing 1 c.c. of each evenly over accurately measured squares (usually 60 × 60 mm.) of paper, which was then dried at room temperature. After desiccation the papers were ruled and cut into ten parts each part carrying the equivalent of 0·1 c.c. of serum. In some experiments the sera were dried on cover glasses. Under such conditions it was found there is frequently a marked or complete deterioration of normal isohaemagglutinins, especially within the first four days after drying. Similar results were observed with haemagglutinins in normal human sera for the corpuscles of lower animals. When large amounts of normal agglutinins are present and the carefully dried sera are kept in the refrigerator, they may occasionally escape destruction by desiccation. Natural haemolysins also deteriorate under the influence of desiccation and may do so more than haemagglutinins. For testing blood-groups sera should be kept in the fluid state at low temperature.
W. B.

Teale, F. H. and **Embleton, D. The paths of spread of bacterial exotoxins, with special reference to tetanus toxin.** *J. Path. & Bacteriol.*, 1919, **23**, 50.

This paper records the results of experiments in which animals were inoculated subcutaneously, intravenously, or intraneurally with tetanus toxin or emulsions of cultures. Although they confirm the older view that tetanus toxin ascends by way of the axis cylinders, they show that it also passes to a great extent to the cord by the perineural lymphatics. If these paths are obstructed the occurrence of tetanus may be prevented. By injection of tetanus toxin directly into the blood-stream the authors found that in the space of minutes it had leaked into the peripheral lymphatics to appear in the thoracic duct. The toxin, however, does not pass from the blood into the cerebrospinal fluid, the capillaries of the central nervous system and choroid plexus having apparently a selective function which does not allow the toxin to traverse their walls. Bacteria injected into nerve-trunks can pass through the posterior root ganglia to the cord, although colloidal dyes are apparently stopped in their course along afferent nerves. Tetanus toxin behaves in the same way. As is well known, iodine mixed with tetanus toxin renders the latter non-toxic by the subcutaneous route. The authors find, however, that when injected intracerebrally typical cerebral tetanus is produced. With regard to the site of action of tetanus antitoxin they consider that this is in the circulating blood or at the seat of production of the toxin only, as it cannot be demonstrated to have entered the central nervous system either by way of the blood-vessels, neural lymphatics, or actual nerve substance. Tetanus toxin already fixed in the central nervous tissue is beyond the reach of anti-tetanic serum administered therapeutically. W. B.

Hektoen, L. and **Corper, H. J. The influence of thorium X on antibody formation.** *J. Infect. Dis.*, 1920, **26**, 330.

Experiments on rabbits to determine whether thorium X, which reduces the number of leucocytes, has any influence on antibody production. For the production of antibody one dose of 25 c.c. of sheep's blood was used as antigen, and it was administered either several days after the marked reduction of leucocytes had been effected by large doses of thorium X, or during the administration of the thorium X. The results show that haemolysin production was apparently not interfered with, although the usual amounts of precipitins were reduced. This is probably due to the action on the mechanism of production, as the thorium seems to have no effect on the amount of precipitin if injected when the precipitin production is well under way, about the sixth day after the injection of the antigen. W. B.

Eisler, M. Ueber den Einfluss von Präzipitin auf Toxin-Antitoxin-Verbindungen. [**On the influence of precipitating serum on toxin-antitoxin union.**] *Centralbl. f. Bakteriol.* (&c.), I. Abt., Orig. 1920, **84**, 46.

Some years ago Dehne and Hamburger, and Landsteiner and Prasek, showed that when specific precipitin is brought into contact with another serum containing antibodies there is a loss of the latter, and this loss may be manifest although there is no visible precipitate. The present author has made further experiments on this question and shows in the case of tetanus toxin-antitoxin neutral mixtures, for example, that the addition of certain precipitating sera will render a neutral toxin-antitoxin mixture toxic again. A good deal depends, however, on the nature of the toxin and the duration of union of toxin-antitoxin. In the case of tetanus toxin-antitoxin the union may be interfered with after half an hour if precipitin be added, but will not occur after one hour. In the case of diphtheria toxin-antitoxin or vibrio Kadi-Kjö haemotoxin-anti-haemotoxin the addition of a specific precipitating serum after even half an hour is unable to lower the antibody neutralizing concentration and set the toxin free, although even here some change has been produced. This is shown by the fact that acids can set free toxin from the precipitate. The treatment of tetanus antitoxin with formalin does not prevent the loss of antitoxin in the presence of precipitin. W. B.

Tadokoro, T. Ultraspectroscopic studies on blood serum. I. The antagonistic action of salt in blood serum. *J. Infect. Dis.*, 1920, **26**, 1.

Tadokoro, T. and **Nakayama, Y. Ultraspectroscopic studies on blood serum. II. The difference in the colloidal state of normal and immune serum.** *J. Infect. Dis.*, 1920, **26**, 8.

These papers are concerned with the spectroscopic examination of colloidal solutions. In particular the change in the colloidal state of serum during the antagonistic action of salt is investigated. A hydrogen tube was used, and a quartz cell filled with a mixture of serum and salt solutions. It was found that a change in state of a colloidal serum produced by $CaCl_2$ was reversed by NaCl: and $ZnSO_4$ by $CaCl_2$ or NaCl. It is concluded that the antagonistic action is caused by a reversal of the dispersion of the serum and of the change of the form and structure of particles, for in the experiments the same serum of the same concentration was used.

In the second paper the authors say: 'In the literature on immunization many reports are found which state that the actions of immune serum are intimately related to the colloidal state of the serum.' This has led them to examine the difference between the sera of different animals. They worked with those of the dog, guinea-pig, rabbit, and horse, dealing with the absorption band between 2,950–2,400 mikrons.

It was found that the absorption band of immune serum between the above limits was much longer and larger than that of normal serum.

W. A. M. S.

Teale, F. H. and **Bach, E.** **The relation of the antitryptic titre of the blood to bacterial infection and anaphylaxis.** *Proc. Roy. Soc. Med., Path. Sect.*, 1920, **13**, 43.

This is a record of the variations in the antitryptic titre of the blood in animals during various stages and degrees of bacterial infection and anaphylactic shock. The authors conclude that there is no relationship between the antitryptic curve and the intensity of the infection, pathogenicity, or virulence of the microbes employed. There is also no relation between the antitryptic curve and the toxicity of the infecting microorganism. It is considered that the experiments negative the view of Jobling that the toxaemia in a bacterial infection is due to the formation of toxic proteoses subsequent to the removal of the antitryptic inhibition on the autolytic ferments of the plasma. The authors also believe that Wright's hypothesis of the viability and consequent infectivity of certain microbes being due to the removal of the antitrypsin inhibition with consequent formation of protein degradation products for their growth is incorrect. They consider that the primary factor in the tissues is the reaction and this, with consequent autolysis, favours the growth of the infecting agent. W. B.

Teale, F. H. and **Bach, E.** **The nature of serum antitrypsin and its relation to autolysis and the formation of toxins in infection and anaphylaxis.** *Proc. Roy. Soc. Med., Path. Sect.*, 1920, **13**, 5.

This is a long record of experiments from which the authors arrive at the conclusion that the antitryptic effect of serum is protein in character and not lipoidal, as was held especially by Jobling and Petersen; that it is not adsorbed by bacteria or colloids. There is a weak proteolytic ferment in the serum. It is destroyed by heat at 56° C. and by weak acids and alkalies. This ferment does not influence tissue autolysis, which is quite slow under conditions of complete sterility. W. B.

Widal, F., Abrami, P., and **Brissaud, E.** Étude sur certains phénomènes de choc observés en clinique: signification de l'hémoclasie. [**A study of the clinical aspects of shock: the significance of haemoclasia.**] *Presse méd.*, 1920, **28**, 181.

In a long and important paper Widal, Abrami, and Brissaud sum up the views of the French school on anaphylaxis. In their classical paper in 1913 these authors adumbrated an explanation of the phenomena of anaphylaxis on a physical basis. They now feel able to state this more precisely, and it is significant that in this long paper one finds scarcely any mention of antigen, complement, and all the other hypotheses of the toxic theory.

It has been the fashion for many years to attribute to toxaemia all the effects of the ingestion of harmful substances. The form which the toxaemia took was determined by the nature of the substance administered, i. e. was specific. Of recent years there has been demonstrated, primarily by Richet, a symptom-complex which differs sharply from the toxaemias in that it may follow the administration of any one of a large number of dissimilar substances of either animal or mineral origin. This complex is anaphylactic shock.

Anaphylactic shock is accompanied by dyspnoea, fall of blood-pressure, collapse, vomiting, or other gastro-intestinal troubles, and convulsive phenomena. These are accompanied or preceded by a 'blood crisis' of remarkable suddenness and intensity, characterized by leucopenia with predominance of lymphocytes, diminution of blood platelets, and great alterations in coagulability. Such is the basis on which the symptoms of anaphylaxis are erected. They differ to some degree in intensity and form in different individuals, indeed the form which they will take is rather specific to the individual than to the substance administered, but in all cases there is the same underlying disturbance of serum or cytoplasm. To this disturbance Widal and his co-workers propose to give the name 'crise hémoclasique', and they add to its characters the 'aspect rutilant' of the venous blood and sharp variations in the refractometric index of the serum.

The haemoclasic crisis can be followed with accuracy by means of repeated clinical and blood examinations, and various examples are given of cases in which this has been done. They are as follows: viz. an attack of asthma brought on by the proximity or exhalations of sheep; urticaria induced by ingestion of a particular food, namely, animal albumins, and in other cases by eggs, by fish, and by chocolate. In all these cases some degree of sensitization is presumed to have occurred by previous ingestion of the same articles. But this is not an essential preliminary for the production of an haemoclasic crisis. Such may be induced by massive doses of serum, by intravenous injection of microbic products, or even by injections of milk, such as have been used therapeutically. Nor is it only animal products which are capable of causing the crisis; salvarsan, common salt, and sodium bicarbonate solutions may at times cause a haemoclasia.

There are certain conditions in which haemoclasia occurs in which the influence of a foreign substance is absent or indirect. These are malaria, paroxysmal haemoglobinuria, and wound shock. In the first we may incriminate the sporozooites, in the second the patient's own proteins are so altered as to become 'foreign', and in the last the absorption of abnormal proteins from injured muscles are the potent factors. In some states an even more remarkable condition of affairs is seen, for a purely physical factor such as cold is capable of initiating the cycle of changes to which is given the name haemoclasis, and which is the basis of the clinical condition which we name anaphylaxis, serum disease, asthma, &c., according to the precise reaction which dominates the clinical picture.

Widal, Abrami, and Brissaud would define haemoclasia as a sudden dislocation of the static equilibrium of the colloids of the blood. In support of this view of the phenomenon as a purely physical manifestation they quote the significant fact that many if not most of the foremost authorities on this subject, Besredka, for instance, and as long ago as 1907, have been unable to avoid the same conclusion. Secondly, it is known that very simple chemical substances may bring it about, especially if administered in large amounts, both of which suggest a physical process. Although it is not mentioned, it seems very possible that consideration of the rigors which have followed injection of distilled water would tell in the same direction. Thirdly, there is no doubt that changes occur in the plasma which we can only estimate by methods which are those of pure physics, e.g. alterations in surface tension, conductivity, viscosity, index of refraction, &c. Finally, it is difficult to envisage the action of cold except as producing physical changes, and cold can undoubtedly induce haemoclasia.

It is interesting, one had almost said curious, to find these authors explaining the actual haemoglobinuria of paroxysmal haemoglobinuria by the old hypotheses of complement, antibody, &c., i.e. as a chemical reaction, while the rest of the changes of this disease are quoted as evidence of the physical basis of haemoclasia. We may hope in a subsequent paper to find it admitted that haemoclasia—breaking of the blood—may also include breaking of the red cells, not only in haemoglobinuria *a frigore*, but also in malaria, &c.

Analysed as a physical phenomenon, haemoclasia appears to be essentially a disturbance of the colloid state. The word 'colloidoclasie' is coined to emphasize this fact. So little is at present known of the physics of colloids that the change cannot be further defined. But we are approaching at least a state of knowledge which will permit us to apply physical tests with a view to ascertaining whether the plasma colloids are in a satisfactory state of equilibrium.

In summarizing their paper, Widal, Abrami, and Brissaud make two further points of interest. First, it will be noted that the paper deals almost entirely with the blood, a tissue which is susceptible to study. But this must not be held to imply that the colloidal equilibrium of other sorts of cytoplasm is more stable or immune to noxious influences. It may well be that certain diseases characterized by recurring crises, e.g. epilepsy, have as their basis a colloidoclasia of certain definite groups of cells in the central nervous system or elsewhere. In fact, when we once envisage some such physical basis for symptoms, the field of discussion widens out in a way that has not yet been dreamed of except by the few. Is it not at least probable that every single example of that process to which we give the name 'rigor' is an instance of colloidal disequilibrium?

Secondly, the idea is emphasized that we are approaching on this road a coherent consideration of the problems of personal idiosyncracy. It is not every one who can be rendered sensitive to such influences as the exhalations of horses or the poisons of Rhus toxicodendron. If we envisage this sensitiveness as dependent on a fundamental instability of colloidal equilibrium, as a problem perhaps of precipitation and absorption, we have still many difficulties to face, but we have a clearer direction than has been attained from any other viewpoint. G. W.

Cramer, W. On sympathetic fever and hyperpyrexial heat-stroke. *Brit J. Exper. Path.*, 1920, **1**, 31.

In previous papers the conception has been developed that the thyroid and adrenal glands working together form a humoral apparatus for the heat regulation of the body (see *Medical Science*, 1919, **1**, 117). Their functional activity produces a continuous sympathetic stimulation which leads to increased heat production through mobilization of the live glycogen which is passed into the blood-stream and oxydized. This may be balanced by increased heat loss due to the raising of the hairs of the coat as the result of the stimulation of the arrectores pilorum. Or with more active secretion of adrenalin there is constriction of the cutaneous vessels and diminished heat loss. Thus fever results, which from its origin it is proposed to call 'sympathetic fever'. In man and a few animals, such as the horse, the function of the hairy coat in regulating the heat loss is taken on by the sweat glands.

A short but very virulent 'sympathetic fever' of this type can be produced by the subcutaneus injection of B-tetrahydro naphthylamine. With appropriate doses the temperature rises within one hour after the injection and the animal dies in hyperpyrexia with convulsions and deeply-congested lungs. If the animal survives the temperature returns to the normal level in 4–5 hours. But the dose necessary to produce this effect depends on the climatic conditions under which the animal is being kept. Thus a dose which will kill a mouse kept in a warm room in hyperpyrexia within one hour will have little or no effect on a mouse kept in a cool room. Again, a dose which has little or no effect on a mouse kept in a warm room by itself, will produce a rapidly fatal hyperpyrexia if ten or twelve such animals are crowded together in a cage. It is argued, therefore, that this condition is an 'experimental heat-stroke', and that in its features and post-mortem findings it presents a striking resemblance to hyperpyrexial heat-stroke in man. It is pointed out that this condition of experimental heat-stroke is different from the rise of temperature terminating in death which can be produced in a normal animal by exposing it to a hot environment.

The explanation of hyperpyrexial heat-stroke in man is therefore that an extrinsic factor, namely, deficient cooling due to the conditions of the environment, acts upon an organism which is under the influence of a hyperactive sympathetic system. This latter results from a breaking down of the restraining mechanism which normally inhibits the activity of the thyroid-adrenal apparatus when an organism is placed in a warm environment.

The bearing of this view on the treatment of heat-stroke is discussed. The importance of drastic cooling in the early stages of heat-stroke as a prophylactic treatment is emphasized. As accessory methods the use of chloral and anaesthetics (ether, chloroform) is recommended as antagonists to sympathetic hyperactivity. Morphine aggravates the condition although it obscures some of the symptoms. Saline infusions are contra-indicated and venesection is only symptomatic treatment. W. C.

Kolmer, J. A., Woody, S. S., and Yagle, E. M. The influence of brilliant green on the diphtheria bacillus. *J. Infect. Dis.*, 1920, **26**, 179.

The authors find that solutions of Grübler's brilliant green are highly bactericidal to diphtheria bacilli in glucose broth, for a dilution of 1 : 100,000 kills them within 5 minutes. The presence of blood and serum, however, lowers the effect very considerably, the bacilli surviving in a dilution of 1 : 100,000 for more than 2 hours. Brilliant green is also very effective on staphylococci. Attempts to rid diphtheria carriers of their bacilli were made. A 1 : 250 solution in distilled water was sprayed three times daily over the fauces of 22 persons and into the noses of 17 persons carrying diphtheria bacilli for 2 or more weeks after an attack of the disease. The dye, which was also instilled into the ears of 10 persons with otitis showing diphtheroids, was non-irritating. The results were negative as far as concerns permanency of cure. Usually, the bacilli disappeared after 1–3 days' treatment, but reappeared again. W. B.

Walker, E. Linwood and **Sweeney, Marion A. The chemotherapeutics of the chaulmoogric acid series and other fatty acids in leprosy and tuberculosis. I. Bactericidal action; active principle; specificity.** *J. Infect. Dis.*, 1920, **26**, 238.

For a very long time chaulmoogra oil has had an empirical reputation in the treatment of leprosy, and during the last few years important advances have been made both in the chemistry of this oil and in improved forms of treatment. Chaulmoogra oil is a fixed oil expressed cold from the seeds of *Taraktogenos* (*Hydnocarpus*) *Kurzii*, King, a Burmese tree, and consists essentially of glyceryl triesters of fatty acids. According to Power, although these fatty acids have the same empirical formula as those of the linoleic series, they differ entirely in that their atoms are arranged in a closed carbon chain or ring, i. e. they are cyclic compounds instead of being aliphatic or acyclic like other fatty acids. Two fatty acids of this cyclic series have been isolated and named chaulmoogric and hydnocarpic acids respectively. The present important research of Linwood Walker and Sweeney is concerned entirely with the study of the antiseptic and bactericidal actions of the oil itself and its constituents, the identification and isolation of the active substance, the determination of the specific character of the bactericidal action for acid-fast bacteria, and an investigation of the presence or absence of this bactericidal substance in cod-liver and other oils. The acid-fast bacilli employed in the tests were *B. leprae muris* (Hollmann), *B. leprae hominis* (Levy), *B. smegmatis*, *B. lymphangitidis bovis* (Traum [1]), *B. tuberculosis* (avian, bovine, and human types). In addition, many of the *Streptothriceae* were used as well as *B. typhosus*, *B. coli*, *B. dysenteriae Shiga*, *B. pestis*, *V. cholerae*, *Staphylococcus aureus* and many others. It is shown that the sodium salts of the total fatty acids of chaulmoogra oil have a very high inhibitory and bactericidal action on acid-fast bacilli extending to a dilution of about 1 : 100,000 for the bactericidal effect and 1 : 1,000,000 for the antiseptic effect. The bactericidal dose is about 100 times more active than carbolic acid. The actual active agents of the oil are the chaulmoogric and hydnocarpic acids and possibly lower isomers of the series. The bactericidal activity is shown to be specific for acid-fast bacteria and is not manifest when other bacteria are employed. The group specificity, according to the authors, is probably connected with the fat metabolism of the acid-fast bacilli which are known to contain large quantities of fat. As the authors were unable to demonstrate any morphological or staining alteration in acid-fast bacilli exposed to strong concentrations of sodium chaulmoograte they cannot agree with Rogers, who suggested that there was probably some injury of the protective fatty capsules of acid-fast bacilli. They explain the action as being due to the fact that the fat-elaborating bacilli attempt to utilize the chaulmoogric acids to build up their fatty capsules, and that these cyclic fatty acids contain a group of atoms which is toxic for the bacterial cell. The specific bactericidal activity against acid-fast bacilli is a function of the carbon ring structure of the molecule of the chaulmoogric acid series which so far as is known is found only in chaulmoogra oil and in the oils of certain plants closely allied to *Taraktogenos Kurzii*. The authors were unable to demonstrate the specific bactericidal effect on acid-fast bacteria when the fatty acids of cod-liver oil were employed, although Rogers has made such a claim. They consider, however, that the demonstrated activity of the chaulmoogric acids on all acid-fast bacteria, together with the favourable reports on leprosy, furnish theoretical arguments for the trial of chaulmoogrates in tuberculosis. Animal experiments in this direction are now being carried out and will no doubt be published later.

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[1] *J. Amer. Vet. M. Ass.*, 1919, 55, 639.

W. B.

Kolmer, J. A. and **Idzumi, G. Chemotherapeutic studies with ethylhydrocuprein and mercurophen in experimental pneumococcus meningitis in rabbits.** *J. Infect. Dis.*, 1920, **26**, 355.

The experiments detailed in this paper were carried out in an attempt to obtain better results in the treatment of the very deadly pneumococcic forms of meningitis occurring primarily or secondarily. The high pneumococcicidal activity of ethylhydrocuprein hydrochloride of Morgenroth and 'mercurophen' (sodium oxymercury ortho-nitro-phenolate of Schamberg, Kolmer, and Raiziss) were tested as regards their curative effects on meningitis produced in rabbits by the subthecal injection in the lumbar region of highly virulent cultures of pneumococci types I and II. In the first place it was found that both drugs employed were slightly more toxic by the subthecal than by the intravenous route. Ethylhydrocuprein hydrochloride in a dose of 0·03 to 0·05 grm. per kilo produces leptomeningitis by itself and is lethal in 48 hours. In a dose of 0·5 c.c. of a 1 : 1,000 sol. per kilo weight it produces no deleterious effect. Mercurophen in doses of 0·002 to 0·004 grm. per kilo introduced intrathecally is lethal and causes meningitis, whereas 1 c.c. of a 1 : 2,000 dilution is harmless.

In dilutions of 1 : 4,000 both drugs are germicidal *in vitro* when applied to pneumococcic purulent spinal fluids. When a meningitis has been established in rabbits by pneumococcic cultures, ethylhydrocuprein in amounts of 0·5 c.c. of 1 : 500 and 1 : 1,000 solutions per kilo of body weight showed a beneficial effect provided the drug was administered not later than 4 to 6 hours after the culture and when the culture had only moderate virulence.

Mixtures of specific antipneumococcus serum and ethylhydrocuprein were not superior to the quinine drug alone. Exposure of virulent pneumococci to sodium oleate, as recommended by Lamar, increased their susceptibility *in vitro* to ethylhydrocuprein, but this effect was not noted *in vivo*. Mercurophen solutions were without appreciable action. The authors think that the use of ethylhydrocuprein in man is justifiable provided the drug is injected intrathecally early in the disease. It would appear safe to inject 0·5 c.c. of a 1 : 1,000 dilution per kilo of weight once or twice in 24 hours for a period of several days following the removal of the infected C. S. F. The dose of ethylhydrocuprein advised would amount to 30 c.c. of a 1 : 1,000 solution for a young adult weighing 60 kilo. This is equivalent to 0·0005 grm. per kilo, i. e. at least 60 times less than the toxic dose. W. B.

Fiori, P. Infezioni gassose. [**Gas infections.**] *Arch. ital. di chir.*, 1920, **1**, 383.

Fiori contributes an important article of 262 pages, including the description of a very complete study of sixty-nine cases of gas infection and dealing with that disease on the broadest possible basis.

Part I. Fiori comments on the defects of the numerous schemes of classification which have been suggested for this disease, many of them resting on clinical or anatomical grounds without sufficient regard to bacteriological considerations. As an inevitable consequence, forms which are aetiologically distinct are often found grouped together. A broader basis of classification is needed in order to avoid errors of this kind. Laboratory experiments have proved that in addition to anaerobes which are highly pathogenic in themselves, other germs are met with in gas infections which are innocuous or pathogenic in an indirect way only. The former are the agents of true gas infection; the latter, of ordinary septic processes, which vary in virulence and are at times capable of producing symptoms, such as gas production, oedema, and tissue necrosis, which it is possible to mistake for those of true gas infections on cursory examination. A primary desideratum, therefore, in projecting any scheme of classification, is to mark this distinction clearly, and Fiori does this by dividing gas infections into two main classes: (1) the classical gas infection and (2) infections associated with putrefactive gas formation. The former may at times present characters of putridity, but such would always imply an association with putrefactive saprophytes. In accordance with this classification Fiori proceeds to give a detailed description of the several forms of gas infection, their clinical and anatomical characters and post-mortem appearances. In the first main division are included gas gangrene and gas phlegmon. With regard to the former the clinical and anatomical picture suggests that it habitually assumes one or other of two forms, the emphysematous and the oedematous. In cases where a single germ is present, as exceptionally happens, this suffices to explain the form assumed; where the infection is mixed the form will depend upon the predominance of one particular germ. It is important to note, however, that the same species of germ is capable of producing at one time the emphysematous form, at another the oedematous; and that two diverse species, acting independently, may give rise to an intermediate or mixed form, the oedemato-emphysematous. Infections comprised in the second main division, namely, those associated with putrefactive changes, are treated upon lines similar to the foregoing and in equal detail. These cases form a group which the author was unable, on clinical ground alone, to distinguish from true gas infection, owing to the close resemblance of the symptoms to those of the latter disease.

Part II treats of the causes and modifying factors, extrinsic and intrinsic, of true gas infection. Climatic and geographical conditions, the nature of the wound and projectile, the anatomical peculiarities of the wounded part, and the bacterial factors involved are among the main subjects discussed. The action of individual germs is difficult to estimate, since more than one species is as a rule present in a wound. The difficulty is increased owing to the capacity possessed by some micro-organisms, innocuous in themselves, of becoming virulent when associated with various chemical substances or other germs. And even as regards pathogenic germs, it is recognized that the presence of the germ is not the sole factor in infection. Thus the bacillus of Welch is able to exist saprophytically in granulating wounds, but induces a gangrenous inflammation in the necrosed tissues of lacerated wounds. The supplementary causal factor in such cases has been looked for in the varying action of phagocytes and the tissue fluids, but the difficulties of the problem are, in Fiori's opinion, more fully met by the theory developed by Teale and Embleton, that the degree of intoxication is dependent on the extent of decomposition of the bacteria themselves by supposed tissue ferments, intermediate toxic products being formed. Absence of the ferments or complete destruction of the bacteria by their presence in abundance would imply absence of intoxication; while in intermediate conditions the unhindered proliferation of the germs and their active destruction by the tissue ferments would furnish an abundance of poisonous products. By this theory the acquisition of virulence by non-pathogenic germs, the receptivity to infection in refractory animals, and the action of bacteria in association are rendered comprehensible.

Part III deals with the bacteria of gas gangrene and gas phlegmon. Up to the year 1892 the *Vibrion septique* of Pasteur was held to be the sole causal agent of gas infection. In that year Welch isolated the *B. aerogenes capsulatus* (*B. perfringens*), and thenceforward the notion of the aetiological unity of the disease was abandoned. In order to obtain a precise definition of the characters and properties of these two bacteria for the purpose of identification and diagnosis, Fiori submitted several strains, obtained from reliable sources, to an exhaustive examination, studying their anatomical characters, colonies, staining properties, sporification, mobility, cultural characters, resistance to heat, biochemical properties, products, and immunizing reactions. Two strains of the bacillus of *charbon symptomatique* were studied in a similar way.

Of the germs discovered during the war period, and from time to time regarded as specific of gas infection, descriptions are given based on the records of the original observers and in part on Fiori's own observations. Among these the *B. oedematis maligni* of Novy, first isolated from the guinea-pig in 1894, attracted special attention, and was by some regarded as one of the most frequent causes of gas infection: others are the *B. bellonensis*, *B. oedematiens*, B. of gas oedema (Aschoff), *B. fallax*, *B. aerofoetidus*, *B. histolyticus*, *Streptococcus anaerobicus*, *B. sarcoemphysematosus hominis*, and *B. tumefaciens* (Wilson). A comparison of the characters of these micro-organisms permits of their being arranged in three classes—(1) the *Vibrion septique* group, (2) the *B. perfringens* group, and (3) the bacillus of Novy group.

Among the aerobic germs described from time to time as the specific agents of gas infection, the *B. septicus aerobicus* of Legros and Lecene, from a case of gas gangrene which was fatal in three days, furnished a pure culture which produced, in the guinea-pig, anatomical and clinical phenomena comparable to those of gas gangrene.

Part IV includes the descriptions of Fiori's own cases, prefaced by a critical examination of method and technique. The researches were based on a study of the blood, the tissues of the wound, and the viscera; and as regards the first of these, the methods of endoperitoneal inoculation in the guinea-pig and haemoculture were made use of as far as possible. In 36 fatal cases the results of haemoculture were positive in 27. In 11 non-fatal cases, 5 gave positive results, the germs isolated in pure culture being non-pathogenic for the rabbit and guinea-pig and exclusively anaerobic; in three of these five cases the *B. perfringens* was also present in the wound, demonstrating the possibility of the passage of non-pathogenic germs into the blood from wounds in which pathogenic anaerobes of the type of perfringens are also present. Fiori concludes from these observations that the presence of pathogenic anaerobes in the blood indicates, as a rule, a fatal termination. The possibility of their existence exceptionally in the blood in non-fatal cases cannot be absolutely denied, and their presence would then be regarded as due to a transitory bacteriaemia, such as occurs at times in cases of grave local pyogenic infection, or to the pathogenic germ being of an attenuated strain.

In discussing the various procedures used in his researches Fiori points out the relative advantages of the methods available, the precautions necessary to ensure success, and the criteria upon which the bacterial identification and diagnosis should be based.

The cases investigated comprise 51 cases of gas gangrene, 5 of gas phlegmon, and 13 putrefactive forms of gas infection, and the exhaustive descriptions given of them are accompanied with excellent photographs of the micro-organisms and their colonies. From a study of the characters and properties of the germs isolated by the method of haemoculture, Fiori divides the cases into five groups, appending to each a brief description of the predominant anatomical characters met with. The micro-organisms isolated in the first group (5 cases) presented resemblances both to the *Vibrion septique* and to the bacillus of *charbon symptomatique*; the second group (6 cases) corresponded to that of the *Vibrion septique*; the third (2 cases) gave negative results with the agglutinating serum of *Vibrion septique* in weak concentrations, feebly positive results in greater concentrations, negative results on neutralization with the antiserum of *B. Charbon symptomatique* and of *B. oedematiens* (homologous with the bacillus of Novy), positive results on neutralization with the antiserum of *Vibrion septique.* Group four (2 cases) showed reactions very similar to those obtained in group three. Group five (10 cases) gave positive results on neutralization with anti-perfringens serum. Fiori concludes that germs of the types *Vibrion septique* and *B. perfringens* have about equal importance in the causation of true gas infections, while those of the bacillus of Novy type take a subordinate place. The investigation of the five cases of infections associated with putrefaction, in which the haemocultures gave positive results, were carried out on lines similar to the above.

By means of haemoculture *in vivo,* therefore, Fiori has been able to separate two main groups of anaerobes; one powerfully and constantly pathogenic for the ordinary laboratory animals, the other of feeble virulence. The former are devoid of putrefactive properties, feebly proteolytic, more or less actively saccharolytic, the latter more or less markedly peptolytic and slightly saccharolytic.

The researches on the tissues of the wound showed that in 44 cases in which the *B. perfringens* was present, whether in association with other germs (35 times) or alone (9 times), the issue was fatal in 21 (47·7 per cent.). The mortality in those cases in which the germ was the sole pathogenic anaerobe present was sensibly lower than in those in which other anaerobes were associated with it. In 21 haemocultures from cases where this germ was present in the wound the results were positive 12 times (57·1 per cent.), and as with the micro-organisms of the first four groups mentioned above, the presence of the germ in the blood was associated with a fatal issue. Six times a germ was isolated from wounds which in its morphological and cultural characters closely resembled the *B. oedematiens.* Associated with the pathogenic anaerobes, the occurrence of anaerobes of feeble virulence, and especially such as possess putrefactive powers, was frequently noted.

Part V deals mainly with the associated action of micro-organisms. There is a tendency at the present time to regard the anaerobes of wounds, more particularly the *B. perfringens*, as essentially saprophytes, which by the associated action of other anaerobes may become virulent. Such a view regards only one side of the question, the possibilty of conferring virulence on avirulent germs. It has been amply proved in the laboratory that it is possible, from material obtained from the wound or blood in fatal cases of gas infection, to isolate in pure culture a germ that is capable by itself of reproducing the disease. Of the series of experiments bearing on this question, those made with non-pathogenic germs cultivated in bile are the most interesting. Fiori found that the germs so cultivated and inoculated into a rabbit or guinea-pig almost always caused death in a few hours. The germ could be obtained from the blood and peritoneum of the animal before death, and proliferated vigorously in the living tissues.

T. W. P. L.

Vernoni, G. Sul tetano postsierico. [**Post-seral tetanus.**] *Arch. ital. di chir.*, 1919, **1**, 153.

Patients infected with the bacillus of tetanus who have been treated with antitetanus serum may subsequently develop symptoms of the disease (**post-seral tetanus**). The symptoms may closely resemble those of untreated tetanus (*unmodified*); but in the majority of cases they are notably altered in character (*modified*). The period of incubation both in modified and unmodified post-seral tetanus may be that of ordinary tetanus; on the other hand, it may be prolonged.

Modified post-seral tetanus. The initial symptoms of ordinary tetanus are trismus or tonic rigidity of the muscles of mastication; spasms of the affected part; or pain in the throat, with dysphagia. Further, an early and constant symptom is spasm of the facial muscles (*facies tetanica*): this symptom, however, is less readily recognized by the physician, and the patient is less conscious of its presence. The initial symptoms of tetanus are, therefore, localized, but this character is of very brief duration and the spasms rapidly become generalized. Modified post-seral tetanus differs clinically from ordinary tetanus in this: that it constantly begins with spasms of the injured part, and that the stage of localized spasm is not transitory, but persists for some considerable time. In mild cases the localized spasms constitute the sole symptom of the disease and spontaneous cure results. Such cases are, however, exceptional, and as a rule the symptoms sooner or later become generalized and acquire all or almost all the features of ordinary tetanus, including its gravity.

Modified post-seral tetanus (treated). If injections of antitetanus serum are promptly administered in cases of post-seral tetanus the subsequent course of the disease is profoundly altered. In cases of slight severity the initial local symptoms are forthwith relieved and cure follows without any generalization. In other cases, of less frequent occurrence, the spasms, while remaining strictly localized to the injured limb, or not extending beyond the opposite limb, are of extreme violence and are prolonged. In the majority of cases, however, a more or less complete generalization is superadded to the local symptoms, though the latter constantly predominate in the clinical picture, the generalized spasms being markedly attenuated and affecting but slightly those groups of muscles which, like the muscles of mastication, are early and constantly affected in ordinary tetanus.

In explanation of the difference in the action of the tetanus toxin in ordinary and post-seral tetanus Vernoni refers to the well-known fact that the toxin generated at the seat of infection and rapidly absorbed into the circulation is unable directly to attack the nervous tissues except at the peripheral ends of the nerves. Thence the toxin travels along the nerves to the centres, and adjacent centres may become successively attacked by contiguity. In ordinary tetanus the toxin absorbed into the blood attacks the peripheral nerves of the whole body at almost the same instant and in equal concentration; consequently the symptoms appear contemporaneously and with uniform intensity. In post-seral tetanus, on the other hand, the antitoxin introduced into the blood renders the circulating toxin more or less completely inert, while at the focus of infection a zone of greater concentration of the poison exists which, partly escaping neutralization, is able to attack the nerve-endings in that situation. The symptoms, accordingly, remain localized, and general spasms due to diffusion of the poison are absent or attenuated. In these cases, however, an extension of the area of contractions can occur through the successive involvement of adjacent centres by contiguity. Thus a local tetanus following wound of the arm may present initial spasms in the shoulder: these may be followed by contractions of the trapezius, the sternomastoid, or the nuchal muscles of the same side. In the event of the circulating toxin being but incompletely neutralized by the antitoxin, the local symptoms will be accompanied by contractions of the muscles of the face, trunk, and more distant parts, and by slight trismus, such contractions being bilateral and symmetrical. In cases, referred to above, in which the spasms of post-seral tetanus, while remaining strictly localized, are characterized by extreme severity, it is probable that the infection is of exceptional virulence.

It has already been mentioned as one of the prominent features of post-seral tetanus that trismus is absent or but slightly marked: this cardinal symptom of ordinary tetanus loses almost all its importance in post-seral tetanus. On the other hand, when cases of post-seral tetanus reach a certain degree of severity, it is almost always possible to recognize some contraction of the facial muscles (*facies tetanica*). These muscles, not the muscles of mastication, furnish the most delicate index of the intoxication. It is probable that the liminal excitability of the facial nucleus is on a lower level than that of the trigeminal nucleus: in other words, below a certain degree of concentration of the toxin the facial nucleus may be affected while the trigeminal nucleus escapes.

Prolongation of the period of incubation. The period may be regarded as normal if the symptoms appear within three weeks from infection; an extension of the period into the fourth week is rare. Preventive injections may cause great prolongation of the incubation, depending on conditions which vary in different cases. At times the antitoxin appears to neutralize the poison as fast as this is formed, and the destruction of the bacilli by the tissues is effected before any marked diminution of this process occurs, a definite cure resulting. In other cases, in which the local conditions are more favourable to the growth of the bacilli, the neutralization of the toxin becomes gradually less complete. In these cases the prolongation of the incubation is not great, generally from one to four weeks, and the tetanus is modified. But here, although the incubation is prolonged, the outburst of symptoms is the direct consequence of the original infection and is therefore properly designated **delayed primary tetanus.** In another group of cases the incubation is prolonged for a considerable time—one, two, or three months—before the disease becomes manifest. The disease may then present the characters of ordinary tetanus or be modified; it may be slight or grave: it may arise without apparent cause (spontaneous), or follow an operation or other traumatism (post-operative or provoked). In these cases a considerable period must have existed, anterior to the outburst of symptoms, during which the body was unprotected, since it is impossible to admit that the protective action of an injection could last much beyond the third or fourth week. During this period the infection remains latent; the micro-organisms, although present, undergo no proliferation, and hence the tetanus which ultimately develops is the indirect consequence of the original infection (**late secondary tetanus**).

From these considerations it might be inferred that the nearer the outbreak of tetanus to the preventive injection the greater would be the tendency to modification in the symptoms; and the more prolonged the incubation, the closer the resemblance to ordinary tetanus. It is true that when the period of incubation is not prolonged much beyond the normal, the tetanus is almost always localized; but when the incubation is prolonged over several months the symptoms are not necessarily generalized. The localization of the symptoms in these latter cases is comprehensible, when the symptoms are mild, on the supposition that the virus has become attenuated through prolonged sojourn in the body. But this explanation is inadequate when the symptoms are severe, and Vernoni considers that such cases are best explained by assuming that a process of auto-immunization has become established by the continuous passage of minute doses of toxin into the circulation. T. W. P. L.

BIOCHEMISTRY

Widmark, E. M. P. Studies in the acetone concentration in blood, urine, and alveolar air. I. A micro method for the estimation of acetone in the blood based on the iodoform method. *Bio-Chem. J.*, 1920, **13**. 431.

The amount of acetone may be estimated in 100 c.mm. of blood by a modification of the Messinger method, the details of which must be consulted in the original. The method is suitable for diabetic cases when alcohol is administered, for alcohol in the blood is not estimated as acetone by this procedure. C. G. L. W.

Sharpe, J. S. The guanidin content of faeces in idiopathic tetany. *Bio-Chem. J.*, 1920, **14**. 46.

Guanidin is thought to contribute to the symptoms of tetany. The amount of diacetyl guanidin found in the faeces in four cases of tetany was 0·075 per cent. of the moist faeces. In six normal cases the average was 0·007 per cent. C. G. L. W.

Raistrick, H. Studies on the cycloclastic power of bacteria. I. A quantitative study of the aerobic decomposition of bacteria. *Bio-Chem. J.*, 1920, **13**, 446.

Fermentations were made in a medium containing inorganic salts, to which histidin had been added.

B. paratyphosus A and *B*, *B. faecalis alcaligenes*, and *B. pyocyaneus* attack histidin and produce ammonia and open the iminazole nucleus.

B. proteus vulgaris only forms ammonia from the side chain of histidin and is not able to attack the iminazole nucleus itself.

These experiments are directed to ascertain which micro-organisms are concerned in the bacterial production of histamin and the mechanism of its formation. C. G. L. W.

Togawa, T. Studies in the metabolic changes in experimental tetany. *J. Lab. and Clin. M.*, 1920, **5**, 299.

In parathyroidectomized dogs, showing typical tetanic symptoms, a condition of acidosis is always observed. The antitryptic power and non-protein nitrogen content of the blood are usually increased.

There is no acidosis in thyroidectomized dogs showing no tetanic symptoms; a slight alkalosis is sometimes noticed. In these cases the antitryptic power and non-protein nitrogen of the blood are unchanged from the normal. C. G. L. W.

Ferry, N. S. and **Hoskins, H. P. Bacteriology and control of contagious nasal catarrh (snuffles) of rabbits.** *J. Lab. and Clin. M.*, 1920, **5**. 311.

Laboratory animals, particularly rabbits, are susceptible to a catarrhal condition known as 'snuffles'. Several organisms are found, but *B. bronchisepticus* is responsible for the majority of infections. *Bact. lepisepticum* is an important aetiological factor, and is probably responsible for many of the acute cases which end fatally. *Staphylococcus albus* is a secondary invader. The streptococcus is not a factor.

The disease can be controlled in a large measure with a vaccine composed of the three most prominent micro-organisms. The sanitary surroundings of the animals must be good. C. G. L. W.

Hoskins, H. P. and **Stout, A. L. Bacillus bronchisepticus as the cause of an infectious respiratory disease of the white rat.** *J. Lab. and Clin. M.*, 1920, **5**, 307.

B. bronchisepticus has been isolated from the nostrils, nasal sinuses, trachea, lungs, and heart-blood of white rats affected with a serious disease of a distemper-like character. Agglutination tests point to the identity of the rat organism and *B. bronchisepticus* from a canine source.

C. G. L. W.

Morse, P. F. and **Crump, E. S. Bacteriology and pathology in six cases of encephalitis lethargica.** *J. Lab. and Clin. M.*, 1920, **5**, 275.

A staphylococcus-like organism has been isolated in primary pure cultures from six consecutive cases dying of encephalitis lethargica. The organism when injected subdurally in rabbits produces a fatal lethargic state. The filtered culture contains a poison which is fatal to rabbits when injected by the intradural route. Evidence points to the poison being a toxin rather than a filtrable virus. Agglutination tests were not conclusive.

The pathological findings showed a low-grade leptomeningitis with oedema and moderate round-cell infiltration; perivascular infiltration of the vessels of the white matter, especially of the caudate and lenticular nuclei, optic thalamus, pons, medulla, and posterior horns of the cord, with resulting oedema and miliary haemorrhages of the surrounding parts. C. G. L. W.

Burge, W. E. and **Burge, E. L.** **Effect of the chlorine substitution products of methane, acetaldehyde, and of sodium acetate on catalase production.** *J. Biol. Chem.*, 1920, **41**, 307.

Catalase is the name given to the enzyme which liberates molecular oxygen from hydrogen peroxide. In their studies upon narcosis, the authors found that narcotics decreased catalase in the blood both by diminishing its output from the liver and by direct destruction of the enzyme itself. They concluded that the diminished oxidation during narcosis might be due to the decrease in catalase. In keeping with the interdependence of catalase and of oxidation, Lusk observed that ingested glycocoll increased oxidation, and the authors found that it produced also a great increase of catalase in the blood. Acetic acid or its sodium salt (related closely to glycocoll chemically) was found to produce a great increase of catalase by stimulating the alimentary glands, especially the liver, to an increased output of the enzyme. This paper is concerned with the effect upon catalase of introducing chlorine into the methane molecule and into the sodium acetate molecule respectively. It is found that the more chlorine that is introduced into the methane molecule, the more effectively does the substance decrease the catalase in the blood. The same is true of chloral as compared with acetaldehyde. The catalase is decreased by direct destruction of the enzyme and by diminishing the output from the liver. On the other hand, the increase in catalase produced by ingestion of sodium acetate is made less by the introduction of chlorine into the molecule. The experiments are suggestive in connexion with narcosis, and the authors attribute the decrease in oxidation during chloroform and chloral anaesthesia to be due to the decrease in catalase.

R. A. P.

Kerner, G. and **Lesser, E. J.** Die Änderung der diastatischen Wirksamkeit der Froschleber durch starke Durchspülung mit Ringerlösung. [**Change of the diastatic activity of the frog's liver by energetic perfusion with Ringer solution.**] *Biochem. Ztschr.*, 1920, **102**, 284.

Lesser, E. J. (1). Die Zuckerabgabe der Froschleber bei kontinuierlicher Durchströmung mit Ringerlösung. [**The sugar loss of the frog's liver by continued perfusion with Ringer solution.**] *Biochem. Ztschr.*, 1920, **102**, 294.

Lesser, E. J. (2). Der Mechanismus der Zuckermobilisierung durch das Adrenalin. [**The mechanism of sugar mobilization by adrenalin.**] *Biochem. Ztschr.*, 1920, **102**, 304.

These papers are a contribution to the cell metabolism of glycogen, a subject which is a fundamental one in any understanding of diabetes. The following questions are dealt with. Is the ferment, diastase, which breaks down glycogen into sugar in the frog's liver separated in the cell from the substrate glycogen? This has been shown to be the case for the frog's egg cell. Further, how does adrenalin cause the increased sugar production? The problem is tackled in the following way. Diastatic activity is determined by the difference in the glycogen content of a given liver at the beginning of an experiment, and at the end of say four hours' standing in a Ringer's solution. The difference is a measure of the glycogen content. Blood-free frog's liver is shown to have a lower diastatic effect than the liver containing its original blood. Destruction of the structure of the liver cells with distilled water causes a rise in the diastatic activity of the blood containing liver, but has no effect upon the washed liver. Therefore, the difference of the diastatic effect in the washed and unwashed liver is due to the absence from the former of both blood diastase and liver diastase. The sugar formation in the perfusing fluid is shown to be, in general, most rapid at first, confirming the results of other workers. The sugar split off from hour to hour in a perfusing fluid is really the resultant of two factors, and is therefore influenced a good deal by the rate of perfusion. The two factors are, first, the washing out of the ferment from the liver cells, and, secondly, the removal of the products of hydrolysis. The two factors are opposed, as the removal of the products of hydrolysis usually accelerates a ferment reaction. The view that the diminution in diastatic activity in the washed liver is due to the removal of diastase in the perfusing fluid is confirmed by showing the diastatic effect of the perfusion fluid which is at a maximum at first, and diminishes as the perfusion proceeds.

Bang and others have shown that adrenalin increases the sugar production of a perfused liver, an effect which is apparently present when the cell structure is intact. It is shown that the effect of adding adrenalin to a perfusion fluid is to cause a temporary increase in the sugar production. This, when taken with the absence of increased diastase in the perfusing fluid, points to the fact that no fresh ferment is formed by the adrenalin. Adrenalin is only effective in the first dose, and only when that first dose is given within two and a half hours after the beginning of the perfusion. The only exception to this is that the adrenalin may be given with effect after the two and a half hour period, provided that the perfusion is carried on intermittently in such a way that the total perfusion time does not exceed two and a half hours.

The author thinks that these results can be explained as follows. There is an excess ferment present in the normal living cell. It is brought into contact with the glycogen by adrenalin (adrenalin does not increase the diastatic activity of the perfusion fluid when added to it). After the perfusion has lasted some hours the ferment has been largely washed out of the cell, therefore there is no ferment left for the adrenalin to act upon. These experiments are considered to be the only convincing proof of the separation of ferment and glycogen in the liver cell.

R. A. P.

Abelin, J. u. Jaffé, J. Beitrag zur Kenntniss der physiologischen Wirkung der proteinogenen Amine. Über den Einfluss der proteinogenen Amine, Phenyl- und p-oxyphenylethylamin auf den Kohlenhydratstoffwechsel der Leber. [On the influence of the amines, phenyl- and p-oxyphenylethylamins, on the carbohydrate metabolism of the liver.] *Biochem. Ztschr.*, 1920, **102**, 39.

It is interesting to compare this paper with the results of Lesser which are given in abstract above. The authors show that subcutaneous injection into rats of phenylethylamin and tyramin (the amine formed by the removal of CO_2 from the amino-acid tyrosin) influence the carbohydrate metabolism in a characteristic way. After such injections, rats show a marked decrease, if not an absence of, glycogen in the liver. A former observation by these two authors showed that there was an increase in the respiratory quotient $\left(\frac{CO_2}{O_2}\right)$ after similar injections, suggesting that the sugar formed is burnt. It is suggested that substances of this type function physiologically in the same way. R. A. P.

Woodyatt, R. T. An improved volumetric pump for continuous intravenous injections. *J. Biol. Chem.*, 1920, **41**, 315.

It is claimed that this machine allows the simultaneous injection of one or two liquids into one or two discharge tubes. Both liquids may be injected constantly at different rates bearing known ratios, or one constantly at one rate with one or both varying as desired. R. A. P.

Abelin, J. Einfluss von Diïodotyramine und Tyramine auf die Entwicklung von Froschlarven. [**Influence of diïodotyramin and tyramin on the development of tadpoles.**] *Biochem. Ztschr.*, 1920, **102**, 58.

In connexion with the recent discoveries of the constitution of thyrotoxin, the iodine-containing compound of the thyroid, these results are of interest. Tyramin is shown to have some effect in accelerating the metamorphosis of tadpoles. This property becomes markedly increased by putting iodine into the nucleus of the tyramin molecule. R. A. P.

Weiss, M. Die Farbstoffanalyse des Harnes: I. Über die Zerlegung des Harnes in drei Hauptfraktionen als Grundlage der Farbstoffanalyse desselben. [**On the division of the urine into three chief fractions as a basis of pigment analysis.**] *Biochem. Ztschr.*, 1920, **102**, 228.

This paper might be consulted by those who wish to examine the urine pigments in disease. By the use of neutral lead acetate, the urine can be split into three fractions. They are a red or urobilin fraction, a yellow or urochrome fraction, and a fraction containing uncoloured amino-acids, the histidin fraction. The substances giving the diazo reactions are discussed. The urine contains a tryptophane derivative not always identical with the chromogen of urorosein. R. A. P.

v. Groer, F. u. Hecht, A. F. Zur Kenntniss des Adrenalins: I. Über die Änderung der blutdrucksteigenden Wirkung des Adrenalins nach Behandlung desselben mit bakteriellen Producten. [**Studies on adrenalin: I. On the alteration of the effect of adrenalin in raising the blood-pressure, after its treatment with bacterial products.**] *Biochem. Ztschr.*, 1920, **102**, 1.

v. Groer, F. u. Hecht, A. F. II. Über die Änderung der gefässverengenden Wirkung des Adrenalins unter dem Einfluss verschiedener Wasserstoffionkonzentrationen und nach Behandlung desselben mit verschiedenen bakteriellen Producten und Eiweisskörpern. [**II. On the alteration of the vasoconstrictor effect of adrenalin under the influence of varying hydrogen-ion concentration, and after treatment with various bacterial products and proteins.**] *Biochem. Ztschr.*, 1920, **102**, 13.

Marie observed in 1913 that the prolonged contact of diphtheria and tetanus toxin with adrenalin solutions rendered the latter inactive. The causes of this phenomenon have been studied at some length by the writers. A number of factors apparently contribute to the result. In some cases the preliminary effect of adding alkali to an adrenalin solution is an enhancement of the activity of the adrenalin. Two methods were used as indicators of the activity of the adrenalin, the blood-pressure effect by direct intravenous injection in dogs, and the vasomotor effect on the skin of the guinea-pig. The more alkaline the reaction, the more quickly the adrenalin loses its activity. The maximum effect is produced by a solution of an alkalinity $P_H = 7{\cdot}5–8{\cdot}5$ (Sörensen nomenclature), a reaction just upon the alkaline side of the blood reaction. Contact with the nucleo-proteins of bacteria causes a rapid destruction of the activity of adrenalin preparations which is independent of the reaction and of the presence of oxygen. The boiled nucleo-protein has no effect. Nucleo-protein and also other proteins accelerate the oxidation of adrenalin in air, a property also lost on boiling. On the other hand, many proteins and also tuberculin after prolonged contact in the presence and absence of oxygen, may increase the activity of adrenalin, in one case as much as eight times. This may slightly mask the alkaline effect. The action of diphtheria nucleo-protein is the mixed effect of these various factors.

Though it is difficult to say how far these results bear upon the normal physiology of adrenalin in the organism, they show at least that there are chemical possibilities of controlling the effect of adrenalin apart from the mere discharge of the substance into the circulation. R. A. P.

Hindhede, M. Fettminimum. [**Feeding with minimal quantities of fat.**] *Skandin. Arch. f. Physiol.*, 1920, **39**, 78.

Hindhede experimented with two young men who existed for sixteen months on a diet consisting of bread, potatoes, cabbage, rhubarb, and apples, without the addition of fats. It is stated that the individuals preserved full vitality and capacity for work during the period. H. believes that other experiments in this direction have failed to show the unimportance of fats because the diet did not contain the necessary accessory food factors; these were furnished in the present experiments by the fruit and vegetables eaten.

In connexion with these attempts to establish the usefulness of a one-sided diet and to show the possibilities of excessive economy in nutrition, a recent review by Otto Kestner (Cohnheim) (*München. med. Wchnschr.*, 1920, **67**, 458), of publication No. 280 of the Carnegie Institution by Benedict, Mills, Roth, and Smith, 'Human Vitality and Efficiency under Prolonged Restricted Diet', is interesting. Kestner points out that the experiments of the American authors absolutely refute the idea that under-nutrition can ever be of service as a scheme of national feeding, as has been claimed by Hindhede and others. The results of under-nutrition in Germany show only too plainly the disastrous results of such a procedure.

C. G. L. W.

Austin, J. H. and **Van Slyke, D. D.** **Determination of chlorides in whole blood.** *J. Biol. Chem.*, 1920, **41**, 345.

The method of Van Slyke and Donleavy for the determination of chlorides in plasma can only be applied to whole blood with the modification described by the authors in this paper. R. A. P.

Denis, W. and **Minot, A. S. Effect of feeding with calcium salts on the calcium content of the blood.** *J. Biol. Chem.*, 1920, **41**, 357.

Up to the present we have had no accurate information concerning the effect of administering calcium salts on the content of calcium in the blood. The development of a method of estimating the calcium content in small quantities of blood has made it possible to check the changes in calcium content of the blood as the result of feeding with calcium salts. The authors have carried out a series of experiments upon normal individuals as a preliminary to the investigation in pathological cases. The results of giving calcium lactate by the mouth to men, cats, and rabbits have shown that it is impossible in most cases to increase the calcium in the blood in this way. An increase, however, can be obtained in cats and rabbits when the initial concentration of calcium in the blood is low.

R. A. P.

Denis, W. The determination of magnesium in blood. *J. Biol. Chem.*, 1920, **41**, 363.

The authoress has found, by a method which she has worked out for the determination of magnesium in the blood, values from 0·8–3·8 mg. per 100 c.c. of plasma. This included estimations made upon some pathological cases. The more normal cases only varied from 1·6–3·5 mg. R. A. P.

Folin, O. and **Wu, H. System of blood analysis. A simplified and improved method for the determination of sugar.** *J. Biol. Chem.*, 1920, **41**, 367.

This paper is a supplement to their last paper on sugar analysis in blood. R. A. P.

Osborne, T. B. and **Mendel, L. B. Nutritive factors in plant tissues. III. Further observations on the distribution of water-soluble vitamine.** *J. Biol. Chem.*, 1920, **41**, 451.

Several different sources of water-soluble vitamine have been tested under as nearly comparable conditions as possible. Alfalfa, clover, and tomato seem to have given the best results, followed by spinach, cabbage, turnip, and carrot, and then potato. R. A. P.

Emmett, A. B. and **Luros, G. O. Are the antineuritic and the water-soluble vitamines the same?** *J. Biol. Chem.*, 1920, **41**, p. vii.

Voegtlin, C. and **Myers, C. N. Distribution of the antineuritic vitamine in the wheat and corn kernel.** *J. Biol. Chem.*, 1920, **41**, p. x.

Eddy, W. H. Further studies on the use of water-soluble B in the treatment of infant malnutrition. *J. Biol. Chem.*, 1920, **41**, p. xiv.

These three papers may best be taken together.

Emmett and Luros fed natural brown rice to both pigeons and young rats. The rice was the sole source of water-soluble vitamine. It was supplemented for the rats so that the diet was complete in all other respects. On heating the rice for two and six hours respectively in an autoclave the antineuritic vitamine was destroyed while the growth promoting (water-soluble B) was not altered in the same way. The same was apparently true for the vitamines of yeast. On the basis of their experiments, the authors think that the two vitamines are different.

Voegtlin and Myers have found that the removal of the embryo from corn and wheat deprives the food of the antineuritic vitamine as judged from experiments on pigeons. They conclude that this vitamine resides in the germ.

Eddy has confirmed his previous work on the value of adding water-soluble B extract to the diet of infants suffering from malnutrition of the marasmus type, under more quantitative conditions. R. A. P.

Osborne, T. B. and **Mendel, L. B. Fat-soluble vitamine of green foods.** *J. Biol. Chem.*, 1920, **41**, p. vii.

Steenbock, H., Boutwell, P. W., and **Kent, H. E. A correlation on the occurrence of the fat-soluble vitamine.** *J. Biol. Chem.*, 1920, **41**, p. xii.

McCollum, E. V., Simmonds, N., and **Parsons, H. T. The aetiology of rickets.** *J. Biol. Chem.*, 1920, **41**, p. xxxi.

Hess, A. F. The rôle of fat-soluble vitamine in human nutrition and its suggested relation to rickets. *J. Biol. Chem.*, 1920, **41**, p. xxxii.

Osborne and Mendel show how the fat-soluble vitamine may be extracted from spinach leaves and clover by drying at 60° C., extracting with ether and evaporating the oily residue upon starch.

Steenbock, Boutwell, and Kent draw attention to their experiments upon white and yellow maize (reported elsewhere in three abstracts), and again discuss the curious association between fat-soluble vitamine and yellow plant pigment. They point out that the vitamine is not the yellow pigment carotin itself.

McCollum, Simmonds and Parsons, and Hess hold that absence of fat-soluble vitamine is not the only source of rickets, as the result of their experiments on diets shows faults in several other factors. Hess claims to have reared five young infants on a diet containing only a trace of fat-soluble vitamine. He also draws attention to the much greater value of cod-liver oil as a growth stimulant as compared with cream or leafy vegetables. It will be interesting to see the results of these experiments at greater length, but it seems a pity that the actual amount of fat-soluble vitamine fed to the children was not tested in some way. The results of other workers, especially Mellanby, seem to be so clear that it is felt that the contradiction cannot be a real one. R. A. P.

Murlin, J. R. Average food consumption in training-camps of the United States Army. *J. Biol. Chem.*, 1920, **41**, p. xvi.

The average food consumption in 427 messes is 3,633 calories per man. Adding on canteens, an all-round consumption of 4,000 calories is the figure. Neglecting canteen consumption, the food distribution is 14 per cent. protein 31 per cent. fat, and 55 per cent. carbohydrate. As compared with civilian dietaries the percentage of protein is higher, of fat is about the same, and of carbohydrate is slightly lower. The average recruit on this diet gained 7 pounds in 5 months of training. R. A. P.

Langworthy, C. F. and **Deuel, H. J.** **Digestibility of raw corn starch.** *J. Biol. Chem.*, 1920, **41**, 1.

Contrary to accepted opinion the authors have found that three subjects who ate 250 grm of raw corn starch a day for three days had no abnormal symptoms and digested 100 per cent. The starch was given in the form of a frozen custard. R. A. P.

Johns, W. and **Finks, A. J.** **Studies in nutrition. II. The rôle of cystin in nutrition as exemplified by nutrition experiments with the proteins of the navy bean, Phaseolus vulgaris.** *J. Biol. Chem.*, 1920, **41**, 379.

Since the pioneer work of Hopkins, the evidence as to the essential amino acids needed in the make up of a protein for growth and for maintenance respectively has been steadily improving. Totani showed that the place of tyrosin could be taken by phenylalanin. Hopkins has shown that when glutaminic acids and aspartic acids are removed from the products of hydrolysis of a protein which will maintain growth, the resulting amino acid mixture will still maintain growth normally.

Further, Ackroyd and Hopkins have shown that arginin and histidin are to a certain extent interchangeable. There was apparently one contradiction to the view that the value of a protein in nutrition was a question of its amino acids. Osborne and Clapp showed that although phaseolin from the navy bean contained all the amino acids necessary for growth, the protein did not promote growth. There is, however, very little cystin (the sulphur containing amino acid) present. The authors have shown that if cystin is added to the cooked protein, adequate growth is obtained in their rats. This would seem to dispose of the apparent contradiction of the experiments of Mendel and Clapp, and further to indicate the importance of cystin for normal growth. R. A. P.

Henderson, Y. and **Haggard, H. W.** **The influence of oxygen deficiency and related conditions upon the haemato-respiratory functions.** *J. Biol. Chem.*, 1920. **41**, p. xlv.

The normal reaction of the blood (hydrogen-ion concentration) is a result of the relation of $H_2CO_3:NaHCO_3$. More or less alkali is called into the blood to satisfy this relation, so that in normal persons the blood alkali is controlled by the dissolved CO_2. The amount of dissolved CO_2 in the blood is controlled by the pulmonary ventilation, which in normal persons is adjusted to the oxygen partial pressure of the air in which the person is living. If over-breathing is induced, the H_2CO_3 of the blood is reduced and so is the $NaHCO_3$, by passage of alkali out of the blood. This condition is termed the acapnial process and is said to be the condition of carbon-monoxide poisoning. It is distinguished from acidosis in which the blood alkali is neutralized and passes out through the kidney. A test to distinguish between the condition of diminished blood alkali in the whole body and the acapnial condition, which amounts to a retention of alkali in the tissues is to administer air with 8-10 per cent of CO_2 in it. This will cause death in the true acidosis, but will restore the acapnial subject to a practically normal state by recalling to the blood alkali from the tissues. The authors have applied this treatment to certain of the latter cases after surgical operations with success, and also obtained beneficial results in dogs asphyxiated with carbon-monoxide. R. A. P.

Myers, V. C. and **Killian, J. A. Chemical changes in the blood in advanced nephritis.** *J. Biol. Chem.*, 1920, **41**, p. xx.

Myers, V. C. and **Kast, L. Glycosuria in three cases of chronic nephritis with oedema but with only slight nitrogen retention.** *J. Biol. Chem.*, 1920, **41**, p. lxi.

As creatinin is the nitrogen compound most readily excreted by the kidney, it is the last to be retained in nephritis. This fact combined with the constancy of the amount of creatinin produced by the body (creatinin being of endogenous origin) makes the amount of creatinin in the blood a most valuable prognostic test of renal insufficiency. Of 85 cases showing over 5 mg. per 100 c.c. of blood, the authors had 80 deaths. It is suggested that the methyl guanidin arising from creatinin may be the cause of some of the terminal symptoms.

Myers and Kast report three interesting cases of renal diabetes—a condition resembling in many respects the diabetes produced by giving phloridzin to an animal. This drug makes the kidneys permeable to blood sugar, producing sugar in the urine (glycósuria) independent of sugar in the blood (hyperglycaemia). The method has been a valuable one in the hands of several experimenters in determining the substances which normally give rise to sugar in the organism. The three cases reported showed proteinuria and oedema with little nitrogen retention. One case gave a normal blood sugar, the others showed a slight hyperglycaemia. In one the glycosuria was shown to be completely independent of the hyperglycaemia. The cases apparently bore a very close resemblance to cases of uranium poisoning.

R. A. P.

Burns, D. A note on the effect of purgation on the creatinin content of the urine. *Bio-Chem. J.*, 1920, **14**, 94.

Purgation by Rochelle salts, or the ingestion of copious amounts of water, leads to a slight increase in creatinin in the urine.

Acid sodium phosphate, an acid purgative, leads to a slight decrease in the creatinin. C. G. L. W.

Harden, A. The antiscorbutic properties of concentrated fruit juices, Part III. *Bio-Chem. J.*, 1920, **14**, 171.

A description is given of various methods of obtaining orange juice in a concentrated form. These concentrates preserve their antiscorbutic properties for at least two years when stored in a dry atmosphere at ordinary temperature. The preparation on a commercial scale is quite practicable, and should prove of considerable value when antiscorbutic material is required in a concentrated and stable form. C. G. L. W.

Chick, H. and **Hume, E. M. The production in monkeys of symptoms closely resembling those of pellagra by prolonged feeding on a diet of low protein content.** *Bio-Chem. J.*, 1920, **14**, 135.

This paper gives an account of feeding monkeys with a diet in which the protein was deficient in lysin and tryptophane. The accessory food factors were supplied throughout in the necessary quantity. Owing to difficulties with the diet, there was loss of weight from partial starvation. In the animal consuming most food skin lesions developed with co-extensive localized oedema. The addition of tryptophane to the diet of one case had no effect, staved off death for many weeks in another, and slightly modified the symptoms in a third.

The administration of lysin, arginin, and histidin had no effect.

The addition of 5–10 grm. of caseinogen to the diet of a severe case brought about a dramatic cure. The symptoms brought about by this type of diet closely simulate what is found in cases of true pellagra. The main point in the diet was that it was deficient in proteins of good biological value.

C. G. L. W.

Masters, H. and **Garbutt, P. An investigation of the methods employed for cooking vegetables, with special reference to the losses incurred. Part II, green vegetables.** *Bio-Chem. J.*, 1920, **14**, 75.

Examinations were made of the colour changes, production of volatile acids, volatile sulphides, and the effects of the addition of sodium bicarbonate to the cooking water. The vegetables investigated were cabbage, spring greens, and brussels sprouts. The addition of alkali decreases the time of cooking and diminishes loss. The colour is preserved. In steaming, a small amount of volatile alkali—ammonium carbonate—is useful.

C. G. L. W.

Delf, E. M. Effect of heat on the antiscorbutic accessory factor of vegetable and fruit juices. *Bio-Chem. J.*, 1920, **14**, 211.

Investigations were made of the protective action of cabbage juice, swede juice and orange juice, when fresh and after heating to various temperatures for varying times. There is a reduction of antiscorbutic properties by heating the juices, which is greatest in the case of cabbage juice and least in the case of orange juice. After heating at 100° C. for one hour the protective action of cabbage juice had deteriorated to one-seventh of the original; orange juice was only slightly affected under these conditions. It would appear that heating the juices in the absence of air, as is done in commercial processes, provided the time of heating be short and the temperature high enough to ensure sterility, has less destructive effect on the antiscorbutic and growth factors than heating at a lower temperature for a longer time in the presence of air. C. G. L. W.

Harden, A. and **Zilva, S. S. The antiscorbutic requirements of the monkey.** *Bio-Chem. J.*, 1920, **14**, 131.

A monkey (*Macacus rhesus*) of 2–3 kilos is protected from scurvy by the same quantity of orange juice as a guinea-pig of 300–400 grm. Two months are taken for the development of a scurvy which under similar conditions would develop in three weeks with a guinea-pig. This suggests that the monkey possesses a higher store of the antiscorbutic factor than the smaller animal. C. G. L. W.

Hansen, S. Urobilinuri ved cholelithiasis. [**The relation of urobilinuria to gall-stones.**] *Ugesk. f. Læger*, 1920, **82**, 415–423.

The first results of Hansen's investigations were (1) that, to judge by the literature, urobilinuria may be found in any febrile disease, the apparent capriciousness of its occurrence being the measure of various investigators' ignorance of its character; and (2) that Schlesinger's test, hitherto employed by nearly all investigators, is quite unreliable. Hansen does not describe the test he has elaborated (and published in *Ugeskrift for Læger*, No. 1, 1918,) beyond referring to it as a quantitative test, with standards for comparison graduated 1/10, 1/20, 1/40, and 1/80.

His material consisted of 50 definite cases of gall-stones, and 175 controls. Among the 50 cases were 40 showing urobilinuria; and among these again there were 32 giving a positive reaction corresponding to a standard dilution of 1/20 or a still higher dilution. An instructive feature of the 10 negative cases was the complete absence in 5 cases of any bout of pain during the patients' residence in hospital. This suggests that gall-stones at rest do not provoke urobilinuria. As for the other 5 negative cases, it was found on operation that the common bile-duct was invariably obstructed; by gall-stones in 4 cases and by a tumour of the head of the pancreas in 1 case. In these 5 cases the test for urobilinuria was negative, even in a dilution corresponding to the standard 1/2 which, even in health, usually indicates a positive test. If, in a case of jaundice, the urobilinuria reaction becomes negative even in a 1/2 dilution, and if the jaundice persists, there is strong evidence of complete obstruction of the common bile-duct. And if the absence of urobilinuria persists in such a case, cholaemia with haemorrhage and other toxic phenomena threaten, and every day's delay of operative treatment is dangerous.

With reference to the differential diagnosis of gall-stones and acute appendicitis, 35 cases of the latter were examined for urobilinuria. It was absent in 22 cases, present in a 1/10 dilution in 7 cases, in a 1/20 dilution in 5 cases, and in a 1/40 dilution in 1 case. This case was complicated by pneumonia and jaundice, and all the 5 cases giving a positive reaction with a dilution of 1/20 were severe, but in 3 of them the reaction was not positive till after operation. In another group of 175 mixed surgical cases, 124 gave no reaction, 27 reacted in a 1/10 dilution, and 24 in a 1/20 or higher dilution. But the reaction in several of these latter cases was not positive till after laparotomy had been performed. This often provoked urobilinuria although the anaesthetic used was ether, not chloroform, the administration of which is credited with causing urobilinuria.

The general rules governing the relation of urobilinuria to gall-stones would seem to be these: the mere presence of stones in the gall-bladder does not cause urobilinuria. An attack of gall-stone colic almost invariably increases the excretion of urobilin in the urine, provided the common bile-duct is not obstructed. If this is blocked by a gall-stone and the flow of bile into the intestine is completely arrested, bile-pigment, but no urobilin, is found in the urine.

Hansen expresses great satisfaction with this test, the systematic adoption of which at the Bispebjaerg Hospital has proved of value in the differential diagnosis of various abdominal diseases. In some cases with a negative urobilinuria test, but with a clinical picture typical of biliary colic, operation showed no gall-stones, but duodenal ulcer, cancer of the liver, or some other disease. The reaction is not, however, absolutely specific for gall-stones, and it must be interpreted with discrimination.

C. L.

Hoshimoto, M. The influence of thyroid feeding upon the physiological action of the pancreas. *Endocrinology*, 1920, **4**, 56.

Thyroid feeding in rats produces a diminution of the diastase in the pancreas. There is also, as has been noted before, a diminution of the acidophil granules in the cells of the pancreas and an enlargement of the whole gland.

It is suggested that the steatorrhoea, which has been observed in several cases of Graves's disease, is the result of the action of the thyroid hormone on the pancreas. W. C.

Rohdenburg, G. L. Thyroid diabetes. *Endocrinology*, 1920, **4**, 63.

The author records observations on a group of four patients belonging to the same family: two sisters, the husband of one of the sisters, and one of the two sons of this couple. These four individuals developed diabetes, the two sisters at the time of the menopause, the husband at the age of fifty-six, the son at the time of puberty (18 years). In the course of treatment various types of medication were applied; amongst other drugs, preparations of various endocrine organs were given. No appreciable effect was observed except when thyroid and adrenal were given. The administration of these glands greatly increased the glycosuria. The changes in the output of urinary sugar are described as 'at times uncomfortably startling'.

The after-history of the cases is interesting. The three older patients died. The son developed exophthalmos and had a portion of his thyroid removed. Six months after the operation his urine was sugar-free and was still sugar-free four years later when he came again under the author's observation.

Another case of a woman is reported in which there was first a development of Graves's disease which was treated by removal of one lobe of the thyroid gland. After a temporary improvement (gain in weight, slowing of pulse), she began to lose weight again and developed diabetes. This was followed by a great increase in the pulse-rate. Hyperthyroidism being diagnosed, the other lobe of the thyroid was extirpated under local anaesthesia leaving the isthmus *in situ*. After a temporary increase in the urinary sugar, the urine became sugar-free four days after the operation and had remained so for three months, even after an unrestricted diet.

The observations emphasize the importance of the thyroid gland as a factor in diabetes. W. C.

Sandiford, T. The basal metabolic rate in exophthalmic goitre (1917 cases) with a brief description of the technique used at the Mayo Clinic. *Endocrinology*, 1920, **4**, 71.

The paper gives an account of the routine procedure employed in the Mayo Clinic for the investigation of thyroid disorders. For this purpose the estimation of the basal metabolism of the patient is stated to be of the greatest value, because it gives a very accurate mathematical index of the degree of functional activity of the thyroid gland. The metabolic rate is increased in hyperthyroidism and may rise well over 100 per cent. above normal in exophthalmic goitre; it is diminished in hypothyroidism, and may in myxoedema fall to 40 per cent. below the normal. Beside thyroid disorders there are no diseases that have so far been shown to have a constant and distinct variation from the normal in the basal metabolic rate except disorders of the pituitary gland, conditions of profound inanition and fevers. The method is therefore particularly useful in the differential diagnosis of neuroses simulating hyperthyroidism and true hyperthyroidism.

The normal basal metabolism for every person can now be calculated by means of a formula from the surface area, height, and weight of a patient. The actual basal metabolism is determined by means of a simple method (Tissot's method) which is described in the paper. Both the apparatus and the technique are simple so that thirty estimations have been carried out in a day.

These estimations render it possible to study by quantitative methods the effects of the various treatments applied to cases of exophthalmic goitre: rest in bed, ligation, and thyroidectomy. The results obtained in a large number of cases are given in tabular form and are briefly discussed.

W. C.

Hoskins, E. R. and **Hoskins, M. M. The inter-relation of the thyroid and hypophysis in the growth and development of frog larvae.** *Endocrinology,* 1920, **4**, 1.

Jarisch, A. Über die Wirkung der Schilddrüse auf Kaulquappen. [**On the action of the thyroid on tadpoles.**] *Arch. f. d. ges. Physiol.*, 1920, **179**, 159.

These papers deal with observations on the phenomenon first observed by Gudernatsch in 1912 on tadpoles, that thyroid feeding inhibits the growth of the tadpoles but hastens their metamorphosis. The first paper deals with the effect of feeding on dried anterior lobe of the pituitary gland on normal and on thyroidless tadpoles. Given to normal tadpoles it brings about a precocious metamorphosis. Thyroidless tadpoles, if not treated in any way, remain in the larval form more or less indefinitely. If anterior lobe of pituitary is given a beginning of metamorphosis occurs within twenty-four hours, which progresses somewhat more slowly than in normal pituitary-fed tadpoles.

The experiments confirm the view arrived at by experiments on the higher animals, that the thyroid and pituitary are closely related endocrine organs, and can to some extent, function vicariously.

An extensive bibliography is appended to the paper and the results obtained by various workers with amphibian larvae are summarized as follows:

1. Removal of the thyroid hastens growth, causes hyperplasia of the hypophysis and prevents metamorphosis.
2. Removal of the hypophysis retards growth, retards development of the thyroid, prevents metamorphosis, and retards development of cutaneous pigment.
3. Feeding thyroid or hypophysis (or iodine) to normal larvae hastens metamorphosis.
4. Feeding these same substances to thyroidectomized larvae brings about metamorphosis.
5. Feeding hypophysis to hypophysectomized larvae stimulates growth, but does not cause metamorphosis.
6. Feeding iodine to larvae with both the thyroid and hypophysis removed, causes metamorphosis.

The paper by Jarisch deals with the mechanism by which this effect of thyroid feeding is produced. It is shown by a careful and detailed investigation of the changes which take place in tadpoles, that this mechanism can be explained as being the result of the increased metabolism which thyroid feeding produces. This leads to a more rapid regressive change in larval organs. Their disappearance is in itself responsible in many respects for producing the impression of a more rapid metamorphosis; in other respects it enables processes of metamorphosis to take place. It is therefore unnecessary to assume that thyroid feeding produces a direct favouring effect on the development of the larvae. W. C.

Ransom, F. The restoration of the frog's heart in chloroform poisoning. *J. Pharmacol. & Exper. Therap.*, 1920, **14**, 367.

In cases of heart failure from chloroform poisoning it is desirable that one should have some means of restoring the heart. This paper records experiments on the frog's heart. The heart is perfused with a dilute solution of chloroform: after it has stopped it is perfused by a solution of the same strength of chloroform to which a drug has been added. The pressure used for perfusion would force fluid through the heart, even if its beat had stopped, but in order to obtain equally good results in the human subject it would be necessary to inject the various substances before the heart had actually stopped.

The drugs can be divided into three groups: (1) Those that have no restorative effect: this group contains pituitarin which in a concentration of 0·5 per cent. showed no restorative effect. (2) Those that have a restorative effect but later stop the heart because of their own toxic effect. If, however, they are replaced by fresh Ringer solution as soon as they have restored the heart, it will continue to beat indefinitely. These drugs consist of strontium chloride 0·1 per cent., tincture of strophanthus 0·01 to 0·1 per cent., caffein 0·1 to 0·25 per cent., and diuretin 0·01 to 0·1 per cent., the stronger concentration in each case being the more effective. (3) Those that restore the heart and keep it in good condition for an appreciable interval of time even if the chloroform is perfused with the drug all the time. Adrenalin 1 : 1,000,000, and tyramin 1 : 1,000,000, comprise this group.

H. E. R.

Le Heux, J. W. Cholin als Hormon der Darmbewegung. II. Mitteilung. Zur Erklärung der wechselnden Wirkung des Atropins auf den Darm. [**Cholin as hormone of intestinal movement. II. Communication. On the explanation of the varying action of atropin on the intestine.**] *Arch. f. d. ges. Physiol.*, 1920, **179**, 177.

Investigations on the pharmacological action of atropin on the movements of the isolated intestine have yielded very contradictory results. Some observers found inhibition, others excitation, even with similar doses and under apparently similar conditions. The explanation is to be found in the following facts. The intestine contains a water-soluble substance which can be easily extracted from it by repeated washing with saline. This substance, which consists chiefly of cholin, is one of the conditions for the automatic activity of Auerbach's plexus and is therefore called by the author 'the hormone of intestinal movement'. Its presence or absence determines the action of atropin which is its pharmacological antagonist.

If cholin is present the antagonistic action of atropin produces inhibition. If cholin has been removed by repeated washing, atropin produces its own effect, namely stimulation. W. C.

RADIOLOGY AND ELECTROLOGY

Radiotechnique

Guilleminot, H. Dosage du rayonnement X par la fluorométrie. [**Dosage of X-rays by fluorometry.**] *J. de radiol. et d'électrol.*, 1919, **3**, 440.

Since 1910 the author has used this method of dosage in all his work, notably in the treatment of deep-seated tumours. By varying the distance between the anticathode of an X-ray tube and a barium-platino-cyanide screen the fluorescence excited by the X-rays is equalized with that excited by a layer of radium bromide covered with a sheet of mica. An instrument with the aid of which this can be readily accomplished is described. The distance from the anticathode to the screen is called the 'equivalence' of the tube. A unit of intensity is proposed, being that intensity of radiation which, when normally incident on a 2 per cent. solution of iodoform in chloroform, placed in a cubical cell of 1 cm. edge, liberates 1×10^{-8} gr. of iodine in one second. As a medical unit of quantity (M) the author uses this unit intensity acting for one minute. The radiation from the radium bromide, which weighs about 50 mgr. and is spread over one square cm., is of unit strength, and, therefore, so is that of the X-ray tube at the 'equivalence' distance. Since the intensity is inversely proportional to the square of the distance between the screen and the anticathode, it can be calculated for the distance at which it is desired to work. A special slide rule is used for this calculation. The intensity thus obtained, multiplied by the time in minutes, gives the dose. The high price of radium has led to a modification of the apparatus so that a film of radio-luminous paint can be used as the standard intensity of illumination.

It is stated that, when the dose absorbed by the 1 mm. thick layer of Malpighi, at one séance, is 25 M there is no inflammatory reaction, but with the absorption of 30 or 35 M there is a slight reaction, whatever the character of the radiation. Not more than 75 M should be absorbed per month. A figure is given which shows the variation, with the character of the tube, of the dose which may be administered, so that 25 M is absorbed by the Malpighian layer. With a tube of hardness 4 Benoist, 370 M is sufficient, while 610 M is necessary with a 7 Benoist. Another figure shows the amount of each dose absorbed by a layer of thickness 1 mm. at different depths. J. R. C.

Radio-diagnosis.

Brown, L. and **Sampson, H. L.** **The early Roentgen diagnosis of ulcerative tuberculous colitis.** *Am. J. Roentgenol.*, 1919, **6**, 625.

In a careful paper details are given of the methods adopted by the authors at the Trudeau Sanatorium in administration of barium meals and barium enemata. Attention is focussed upon the condition of the caecum on the ground that the earliest situation of tuberculous ulceration is the neighbourhood of the ileo-caecal valve. Under normal conditions after a standard barium meal they find that the stomach generally empties itself in from three to six hours. The first evidence of barium is seen at the ileo-caecal valve in from one to three hours. The ileum empties itself in from five to nine hours. Barium is first seen in the caecum in from two to four hours and it gradually fills as it receives the contents of the ileum. In the meantime the barium column moves slowly forward until all the barium is in the colon. Six hours after ingestion of the meal the head of the barium column is usually proximal to the splenic flexure. The ascending colon remains well filled from the fourth to the fourteenth hour and often as long as thirty-six hours. Complete evacuation takes place usually in from thirty to forty-eight hours. In the pathological conditions under consideration hypermotility is one of the first things noticed, the barium being completely eliminated in twenty to twenty-four hours, and this hypermotility particularly concerns the caecum and ascending colon. At the same time a ragged outline may be noted for the ascending colon, and filling defects are characteristic. Emphasis is placed upon the fluoroscopic examination, but some plates must be taken in each case to reveal and record certain filling defects. The paper is supplied with good radiographs and a complete list of findings in 175 cases. Of these 44 were positive, 32 doubtful, and 99 negative for tuberculous colitis, while in 28 cases operated upon 27 upheld the radiological diagnosis. W. S. L-B.

PFAHLER, G. E. Malignant disease of the lungs, its early recognition and progressive development, as studied by the Roentgen rays. *Am. J. Roentgenol.*, 1919, **6**, 575.

Pfahler has made an analysis of 242 cases and finds that while primary malignant disease of the lung is rare, secondary disease is common. The latter occurs in four types; nodular, mediastinal with infiltration at the roots, general miliary infiltration, and pleuritic.

When the lungs are involved, Pfahler considers it to be part of a general carcinomatosis, and with few if any exceptions one cannot effect a complete recovery. R. W. A. S.

PARISOT, J. et **DARBOIS, P.** Étude radiologique des poumons et du cœur chez les intoxiqués par les gaz. Son utilité pratique pour le diagnostic rétrospectif de l'intoxication. [**Radiological study of the lungs and heart in cases of gas poisoning. Its practical utility for retrospective diagnosis of the type of gas inhaled.**] *Bull. et mém. Soc. méd. d. hôp. de Par.*, 1919, No. **25** (*J. de radiol. et d'électrol.*, 1919, **3**, 550).

Two types of gas leave persistent, subacute, chronic or cicatricial lesions. These are, suffocating gases such as oxychloride of carbon (phosgene) and blistering gases, such as yperite. A few weeks after poisoning by a gas of the first group the radiological pulmonary image is characterized by (1) accentuation of the bronchial tracts, (2) the presence of dark markings corresponding to congested areas, or of broncho-pneumonia; but in most of these cases, from one to three months after inhalation, these radiological signs disappear almost completely. On the other hand, radiological examination easily demonstrates a cardiac dilatation which may continue for several weeks. Distinctive radiological images correspond to the period of acute poisoning by yperite, which was so much used by the Germans during the last months of the war. On a pulmonary plate that is abnormally clear the bronchi and their branches, the root of the lung and the chain of the juxta-hilary glands, always voluminous, stand out with remarkable clearness and strength. Clear, dark, round spots as large as a millet seed or a lentil, stud the bronchial tracts between the light speckled meshwork of which the pulmonary parenchyma appears to be composed. Later the spots become more definite and darker, while, frequently, dense disseminated or conglomerated areas make their appearance and are capable in this case of involving the whole of one lobe. Lastly, when the lesions are cicatrizing, the image of the lung which was gassed with yperite often remains changed: to the right and left are enormous peri-hilary chains of glands, while the bronchial tracts are very dark, irregular, and spotted; the lungs, oedematous, grey in places, apices oedematous but clearing when the patient coughs; diaphragm arched but surmounted by a band of hyper-clearness due to emphysema of the base. At this period, radiological examination combined with other clinical findings enables one to gauge more precisely the functional capacity of the organs, to appreciate more exactly the lesions due to poisonous gases themselves, and to determine more exactly the degree of disability for pension purposes.

S. U. L-B.

Radiotherapy

Boggs, R. H. The treatment of malignancy by combined methods. *Am. J. Roentgenol.*, 1919. **6**, 481.

This author says it is gratifying to note that all the better surgeons to-day realize that operation is seldom if ever indicated as a palliative measure, and that even in early cases, cutting out the centre of a malignant growth never retards but hastens its progress. Destroying the growth locally by radium, on the other hand, does not hasten the process in the glands. A cure is never obtained unless the disease in the lymphatics is completely removed.

It is generally thought that it is the rays which are absorbed in the tissues and the secondary radiations set up therein that produce the changes. The difference in the physiological action between radium and X-rays may be due to radium giving off Beta-rays, and because the Gamma-rays from radio-active substances set up more intense secondary or Beta-rays than an X-ray tube does. With radium a reaction of much greater degree can be produced without permanently injuring healthy tissue than with X-rays. Radium can therefore be used with a greater destructive power locally than X-rays. Deeper effects can be obtained by placing the source of energy at a distance from the mass to be treated and by cross firing. By placing the radium or the X-ray tube eight inches from the surface and treating through seven ports of entry, a tumour four inches below the surface will receive about the same amount of radiation that the skin of any one area receives. As most malignant cells are about two to five times more susceptible to the destructive action of the rays than normal tissues, it is thus possible to produce retrogression of malignant growths and lymphatic glands some distance from the surface without destroying the skin.

By inserting radium into the growth larger amounts of tissue can be destroyed, but this nearly always hastens metastases, just as in an incomplete operation. The author, therefore, never advises inserting radium into a cancerous growth unless the surrounding lymphatics have been thoroughly treated and the cancerous mass at least partially walled off.

In the treatment of epithelioma, radium and X-rays should always be considered first, because, when properly applied, practically all epitheliomatous tissue will disappear, and there are fewer recurrences than by any other method. It is a perfectly legitimate method of treatment in proper hands, but is liable to abuse if not restricted to its proper field.

In discussing the treatment of epithelioma of the lower lip, the author believes that radiotherapy is at present the best routine treatment, both at the early and late stages, and that surgery and electric coagulation in most cases, should be used as an adjunct. The combination of surgery, radium, X-rays, and coagulation will cure more cases of malignancy of the mouth and throat than any one method alone.

In the treatment of carcinoma of the breast post-operatively the author has adopted the following technique :

(1) To prevent recurrence in the wound and to destroy any foci in lymphatics of the anterior chest wall leading up to the inner clavicular area, the anterior chest wall from the clavicle to an area below the liver should be treated.

(2) The axilla is cross-fired as much as possible and the area below the liver included, the supraclavicular glands are usually involved from the axillary.

(3) The supraclavicular region is divided into four areas, the rays are directed obliquely inward towards the cervical glands ; the rays are directed downward through the shoulder towards the axilla ; directed obliquely downward and backward through the clavicle, and directed obliquely forward from the posterior surface.

(4) The suprascapular area frequently shows metastases. Each should receive a full dose on the affected side.

(5) The mediastinum should be treated both anteriorly and posteriorly through the chest, cross-firing as much as possible, the opposite breast and its main chain of lymphatics should always be treated.

(6) The epigastric region should never be omitted, as this is one of the avenues by which the liver and pelvic viscera develop metastases.

A study of carcinoma of the uterus from commencement to the time the liver and other visceral organs become involved in fatal cases, has shown conclusively that in all cases a combination of radium and X-rays produces the best results in conjunction with the proper surgical treatment. Locally, radium is by far the best form of radiation in this disease.

The author in conclusion says that the combined or selected methods of radium, X-rays, and surgery, when removal is necessary, to-day provide the only rational and efficient means of treating malignancy.

R. W. A. S.

Boggs, R. H. Treatment of goitre by radiation. *Am. J. Roentgenol.*, 1919, **6**, 613.

The medical, radiological, and surgical forms of treatment of goitre are reviewed, and it is pointed out that a small or moderate-sized goitre in an adolescent female is often treated by radiation with marked advantage.

So far as the mode of action is concerned it is asserted that radiation causes a destruction of glandular substance and its replacement by fibrous tissue. The degree to which these changes can be brought about can be made to vary considerably. Much depends upon the proper selection of cases, and this again on recognition of the underlying pathological changes. At the Mayo Clinic they have classified goitre as hyperplastic and non-hyperplastic. Between 1909 and 1913, of 2,917 cases coming to operation, 42·8 per cent. were hyperplastic and 57·2 per cent. were non-hyperplastic. Of the hyperplastic 99·2 per cent. were toxic, i. e. toxic hyperplastic exophthalmic goitre. The indication is to treat these potential exophthalmic goitrous cases of later life in the early stage at adolescence. Clinical observations are made as to the proper method of irradiation in severe cases. The author considers that all forms of exophthalmic goitre derive benefit from X-rays or radium rays, and that some 80 per cent. can be symptomatically cured. As a pre-operative treatment irradiation may also be useful to diminish thyroid over-activity when the tumour is so large as to make operation dangerous. Similarly it is preferable to a second operation in cases of relapse. It is easily understood that colloid, cystic, fibrous or nodular goitres, especially if causing marked pressure without toxic symptoms, do not derive benefit from irradiation. A discussion followed on the paper. W. S. L.-B.

Bordier, H. Le pansement en radiothérapie. Considérations physiques sur les pansements ; conséquences pratiques. [**The dressing in radiotherapy. Physical considerations on the dressings. Practical results.**] *Arch. d'électric. méd.*, 1920, **28**, 7.

In the cleaning and dressing of wound surfaces two physical considerations arise:

(1) The application of any solution that is not isotonic with the tissues will lead to osmotic changes through the walls of the delicate cells exposed. This the author considers to be a cause of pain and to amount to a minute trauma. The evil can be avoided by making the antiseptic solutions isotonic.

(2) Dressings applied wet or dry in the ordinary way become stuck to the wound surface, and the removal causes considerable injury to the delicate granulations, as is evidenced by the bleeding so commonly produced. For this reason the dressing should be kept from the wound by a layer of viscous substance, cream or paste, containing colloidal corpuscles.

It is on these the author particularly relies to effect the desired protection. He advises tincture of iodine or thymol, made up with starch, the resulting compounds being colloidal suspensions. They can be made more viscous by the addition of vaseline or lanoline.

The excuse for his excursion into the surgical province is that the electrotherapist has to apply dressings after X-ray and diathermy procedures, and wishes to obtain the best and quickest healing possible.

N. H. M. B.

Dollinger, B. Quartzlampenbehandlung der Wunden von Amputationsstumpfen. [**Treatment of defective healing in amputation wounds by ultraviolet light.**] *Orvosi Hetil.*, 1918, No. **3** (*Zentralbl. f. Chir.*, 1919, **46**, 230).

From his experience of over 800 amputation stumps irradiated by the quartz-lamp, the author states that very good results are obtained in slowly granulating cases which are not surrounded by dense scar-tissue, and round which there are easily-displaced soft parts. No satisfactory results are obtained by irradiation of tense or badly-nourished wounds in soft tissue. Such cases must be re-amputated. Extensive details are included on the method of treatment and on protection against burning.

S. U. L.-B.

Radium Therapy

GIFFIN, H. Z. Splénectomie pour leucémie myélogène après traitement préalable par le radium. [**Splenectomy for myelogenous leucaemia after preliminary treatment by radium.**] *Med. Rec.*, 1918, **94**, No. 24 (*J. de radiol. et d'électrol.*, 1919, **8**, 378).

The author reports the results of 20 splenectomies at the Mayo Clinic for myelogenous leucaemia, 18 of which had had preliminary radium treatment to the spleen. Under the influence of radium there was a diminution of the size of the spleen, a fall in the number of leucocytes, and an improvement in general health. There was only one operative fatality, giving an operative mortality of 5 per cent., a lower mortality than the average mortality for splenectomies in general. The operative mortality for splenectomies for this disease not previously treated with radium is, according to statistics, 86 per cent. The operative results are thus excellent.

The further results, as the author has noted them, are as follows. Improvement of the general condition appears to be certain, but the operative result from the point of view of survivorship is nil. While splenectomy does not shorten the average duration of the disease, which is 2 to 3 years, in general it does not appear to prolong it.

If the patient is operated on soon after the start of the disease, the post-operative survival is longer, while it is shorter if operation is delayed, the total duration of the disease remaining appreciably the same.

It is probable, says the author, at least in certain chronic types of this disease with fibrosis of the spleen and high leucocytosis, that splenectomy can be considered legitimate, but only from the feeling of well-being it brings to the patient.

R. W. A. S.

MEDICAL SCIENCE

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REVIEWS

LETHARGIC ENCEPHALITIS

Nomenclature. Various synonyms have been suggested as substitutes for 'lethargic encephalitis', but it does not seem likely that any of them will take its place. Lhermitte and Saint-Martin propose the unwieldy term 'primary poliomesocephalitis with narcolepsy' or 'ophthalmoplegic encephalitis with narcolepsy'. Émile-Weil suggests 'Netter's disease' as a comprehensive term to include its many varieties, on the analogy of 'Heine-Medin's disease', though, as Sanz remarks, it would be more just to call it after Economo, who described the first epidemic in Vienna (vide *Medical Supplement*, 1918, **1**, 220 *b*, *et seq*.). Chauffard is in favour of the term 'epidemic encephalitis' originally proposed by Hall. Netter (1), on the other hand, though conscious of its shortcomings, desires to retain the term lethargic encephalitis for the following reasons: (1) The virus of lethargic encephalitis may not attack the brain only, but may also affect the cord and sympathetic. (2) The term 'epidemic' implies that the disease can only exist in an epidemic state, whereas there is no doubt that the disease is spread by sporadic cases apart from periods in which it is epidemic. (3) There are forms of epidemic encephalitis which have nothing to do with lethargic encephalitis. Thus the virus of poliomyelitis may affect the brain exclusively or only a part of it, such as the cortex, mid-brain, or cerebellum.

Historical. Netter (1) points out that the descriptions given by Hippocrates, Aretaeus, and Caelius Aurelianus apply to the present disease. The 'lethargos' of Hippocrates appeared in the cold season, was accompanied by fever, tremor, and delirium, showed a predilection for persons above the age of 25, and often ended fatally, but assumed a more favourable course when abscesses appeared.

According to Durodié, the work of Celsus, who lived in the time of Augustus and Tiberius, contains a chapter devoted to 'lethargic fever', to which the Greeks had drawn attention long ago. Towards the middle of the seventeenth century Sydenham gave the name of 'comatose fever' to cases in which the patients slept for several weeks on end and fell asleep after taking a little fluid. Stahl, in 1779, reported cases of fever, somnolence, nocturnal delirium, strabismus, diplopia, and nystagmus. Similar cases were described by Foinot in 1789, by Pinel in 1802, and by Hourmann in 1837. In 1837, Joseph Franck classified encephalitis into cephalalgic, frenetic, lethargic, and convulsive forms. According to his description, lethargic encephalitis frequently occurred in children and in old persons as the result of epidemics of influenza.

Epidemiology.—Great Britain and Ireland. According to Reece, the total number of cases of encephalitis lethargica notified in England and Wales during the first three months of 1919, the first year in which the disease was compulsorily notifiable, was 283; 41 were notified in London, 209 in urban and 33 in rural districts. The distribution of cases closely followed the aggregation of population, cases being notified in and around London, in the industrial centres of Lancashire, the Potteries, Newcastle-on-Tyne, and in the neighbourhood of Plymouth and Portsmouth.

MacNalty reports an institutional epidemic of encephalitis lethargica which occurred in a home for girls in an English town. Out of 21 inmates there were 12 cases with 5 deaths. A monkey inoculated with material from these cases presented lethargic symptoms and tremors and died. *Post mortem* the brain showed lesions similar to those found in human cases of encephalitis lethargica.

Nesbit, who reports an isolated case in Dublin, states that the disease does not appear to have attracted much attention in Ireland, probably on account of its infrequency. In an article published on March 17 Sir John Lumsden, physician to Mercer's Hospital, Dublin, stated that some 20 or 30 cases had been observed in Dublin.

France. At a meeting of the Académie de Médecine on January 6, Netter (2) drew attention to the recrudescence of lethargic encephalitis in Paris and the suburbs. On February 27, commenting on a case reported by Roblin to the Société Médicale des Hôpitaux de Paris, he stated that there was certainly not a department, and probably not a canton, in France in which there had not been a case of lethargic encephalitis since December 1919, and he added that what was true of France applied to the world at large. In a communication to the Académie de Médecine on March 30, while admitting that in the absence of compulsory notification exact figures could not be given, he estimated the Paris cases at 1,500, and those in the whole of France at about 10,000.

Belgium. In a report to the Académie de Médecine, on February 28, Masoin of Namur stated that lethargic encephalitis, which a year previously had been confined to a few villages in Flanders, was now disseminated throughout Belgium. Cases in Belgium have also been reported by Bouché, Nauwelaers and Meunier, and Lamalle and Leroy.

Holland. According to Cramer of Amsterdam several cases occurred in Holland between April and August 1919, after the epidemic of influenza had subsided, and a similar post-influenzal outbreak took place in March 1920.

Switzerland. The prevalence of the disease in this country is discussed by several writers in the *Schweizer medizinische Wochenschrift*, e. g. Stähelin of Basle, Reich of Aarau, and Kaufmann-Ernst and Maier of Zurich. In a paper published on March 11 Reich states that whereas in the spring of 1919 cases were confined to a few places in western Switzerland, to-day the disease is spread all over the country. Maier calculates that in January and February 1920 there were at least 60–70 cases in the canton of Zurich alone.

Italy. Economo (1) points out that whereas lethargic encephalitis had hitherto given rise to only small epidemics, chiefly of a local character and mainly of interest to neurologists, in the present year a considerable change has taken place. In the Christmas of 1919–20 the disease broke out over the greater part of Italy with such intensity that the sanitary authorities and public became extremely alarmed. In an article published on January 24 Montefusco stated that cases had appeared in Lombardy, Piedmont, Naples, and various southern provinces. At about the same date Oggero stated that the progress of the disease in Italy was causing uneasiness, though strictly speaking there were only sporadic cases and the disease had not appeared in epidemic form except at Verona, where 27 cases with 4 deaths had occurred in December. At a meeting of the Lombardy Society of Medicine on February 13, Baila said that from January 8, when notification of the disease was made compulsory, till February 12 there were 97 cases in Milan. In an article on its appearance in the Trentino, Pergher remarks that the outbreak was not characterized by great diffusion or infective properties, but by its high mortality, since out of 18 cases 6 died. Cozzolino of Parma, writing on February 23, stated that the disease was widely diffused throughout Italy, with special predilection for the north, where its spread was possibly favoured by the damp and cold climate.

Austria. According to Economo (1) about three weeks after its appearance in Italy the disease spread over the Alps in a north-easterly direction and invaded the Tyrol, Upper and Lower Austria, South Bohemia, and South Moravia. Stiefler gives an account of the outbreak in Linz and various districts in Upper Austria in the last week of January and first week of February, and declares that the epidemic was more extensive than that of 1917. The same statement with regard to the outbreak in Vienna is made by Dimitz (2), assistant at the Vienna Neurological and Psychiatric Clinique, to which only 13 cases were admitted in the course of two months in 1917, whereas in the present epidemic there were 71 admissions in five weeks.

Roumania. The occurrence of the disease in Roumania is reported by Marinesco, who gives a detailed clinical and pathological description of a case observed by him in January 1920, and states that he has seen an example of the myoclonic type in a Bulgarian as well as two ambulatory cases.

Spain. At a meeting of the Medical Institute on February 2, which is published in the *Revista de medicina y cirugia prácticas* of March 7, Fornos stated that the disease was generalized throughout Valencia, and an editorial note published in the same number of the journal states that cases had recently appeared in various parts of Spain. Writing on March 12, Sanz stated that the disease was fairly prevalent in Madrid, and was present in other provinces of New Castile, as well as in Old Castile, Estremadura, Murcia, and Eastern Andalusia.

Africa. Cases have recently been reported by Crespin, Dumolard and Aubry, and Ardin-Deltheil and Raynaud (1) at Algiers, by Remlinger at Tangiers, where they occurred during a mild epidemic of influenza, and by Kerassotis at Cairo and Port Said.

India. Stephen and Bulchandani report that the first cases of lethargic encephalitis to appear in India occurred in Karachi in November 1919, the last case occurring on December 10. The epidemic was characterized by an absence of any antecedent attacks of influenza or any other fever, and by an absence of catarrh of the nose or tracheo-bronchial mucous membranes.

United States. Flexner points out that in contradistinction to epidemic poliomyelitis there is no reason to suppose that lethargic encephalitis ever before existed in America. According to W. House, the first case appeared in the United States in the autumn of 1918. By the spring of 1919 cases were being reported throughout the Middle West. The disease reached the Pacific North-West in October 1919, appearing almost simultaneously in Portland, Seattle, and Tacoma.

Canada. Boyd gives an account of an epidemic of 60 cases with 23 deaths which occurred at Winnipeg in October and November 1919. As in the great majority of other outbreaks of lethargic encephalitis, in not a single instance could any connexion be traced between the different cases, and never more than a single case occurred in each household.

Bacteriology. In addition to the researches of Loewe, Hirshfeld, and Strauss, which have recently been abstracted (vide *Medical Science*, 1919–20, **1**, 90, 541–2), reference may be made to the following investigations. Maggiora, Mantovani, and Tombolato, of the Bologna University Institute of Hygiene, isolated from broth cultures of the blood a small Gram-positive diplococcus, which was agglutinated in a dilution of 1 in 100 or even more by the serum of the patient from whom it was isolated, and by that of other patients and convalescents from the disease. It was not agglutinated by normal blood or by the blood of typhoid patients. Guinea-pigs inoculated with blood containing the diplococcus died on the fifth or seventh day after showing a subnormal temperature, paresis of the limbs, intense somnolence, and often muscular jerkings of the limbs, extensors of the nuchal region and vertebral column. At the autopsy haemorrhages were found in all the organs, including the brain and meninges. The brain showed punctiform haemorrhages, especially in the grey substance. Animals inoculated with a 24-hours' broth culture died on the seventh day after showing the same clinical symptoms and anatomical lesions.

Gabri of Alessandria isolated from the blood in three cases an organism which appeared to be a variety of *M. tetragenus*, and concluded that lethargic encephalitis was a septicaemia due to this organism. It should be noted, however, that inoculation of animals proved negative.

S. J. House, of Chicago, isolated a green-producing coccus from the brain in a case in which the blood and cerebrospinal fluid remained sterile. Inoculation of rabbits and guinea-pigs by various routes, including the intracerebral, proved negative.

Pathology. Marinesco regards encephalitis lethargica as a pathological entity possessing an anatomical substratum of vascular origin, consisting in the cellular infiltration of the veins, venules, and capillaries. He thinks that the unknown pathogenic agent is probably conveyed from the throat along the lymphatics up to the mid-brain and medulla, in which most of the lesions are found.

The cerebrospinal fluid. Chauffard remarks that absence of lymphocytosis in the cerebrospinal fluid was at first considered to be characteristic of lethargic encephalitis, but that recently several observers had found a lymphocytosis which might be pronounced (80–100 cells per c.mm.) or slight (20–30 cells per c.mm.). A well-marked lymphocytosis is frequently accompanied by only a moderate excess of albumin (Chauffard, Achard (1), Netter (4), Widal). The practical significance of this, as Achard shows, is that the diagnosis of lethargic encephalitis should not be dismissed in favour of tuberculous meningitis because a meningeal lymphocytosis has been found. The lymphocytosis of the cerebrospinal fluid in lethargic encephalitis is not one of the fundamental characters of the disease, as it is in tuberculous or syphilitic meningitis or in mumps, and is only of short duration. On the other hand, Marie declares that there is too great a tendency at present to mistake a true meningitis for lethargic encephalitis owing to the belief that pronounced lymphocytosis may be found in lethargic encephalitis. In six cases of this disease in which the cerebrospinal fluid was examined by him the meningeal reaction as shown by the lymphocytosis and albumin content was only moderate, and the chemical examination of the fluid made by Mestrezat in one case proved that it was very little different from that of a normal individual.

Netter (3), in reply to Marie's statements, says that his observations had led him to make the following conclusions: (1) At the onset of lethargic encephalitis the number of lymphocytes in the cerebrospinal fluid may be fairly high. (2) During the first few days it may increase. (3) Subsequently it decreases and more or less rapidly reaches a low level. (4) The fall in the number of leucocytes is not permanent and another rise may occur. In conclusion, he pointed out that the general hospital in which his patients were treated was better suited for studying the early stages of the disease than La Salpêtrière, where Marie's observations were made.

Dopter draws attention to the occasional occurrence of an excess of glucose in the cerebrospinal fluid in lethargic encephalitis, and states that when it occurs it may be of diagnostic value. Its presence is to be attributed to a certain degree of hyperglycaemia due to a lesion of the floor of the fourth ventricle. In this respect lethargic encephalitis differs not only from acute meningitis but also from tuberculous and syphilitic meningitis which may simulate it owing to their excess of cerebrospinal albumin and lymphocytosis. In both tuberculous and acute meningitis the glucose in the cerebrospinal fluid is diminished, and in syphilitic meningitis it usually remains normal. Although frequent, however, excess of cerebrospinal glucose in lethargic encephalitis is not constant. In a certain number of cases the amount is normal or even diminished towards the end of an attack.

Excess of glucose in the cerebrospinal fluid was also found by Dumolard and Aubry in 11 out of 12 cases.

Symptomatology. Economo (1) remarks that hardly any other disease shows such a tendency to change its clinical picture as does lethargic encephalitis from epidemic to epidemic, almost every fresh outbreak being characterized by a frequency of symptoms which are seldom if ever observed at other times. The following is his description of a typical case in the epidemic at the beginning of 1920. An *initial stage* could be distinguished characterized by an acute onset, shivering, fever, and neuralgic pains, often of great severity, followed by delirium resembling the occupational delirium of alcoholism, or other psychical disturbances. Severe prostration was often noticed at this stage. The fever was usually slight (99·4–101·4 F.), herpes labialis was frequent. Death might occur at this stage. In a few days a *hyperkinetic stage* developed characterized by myoclonic twitchings of the abdominal muscles, which were first confined to one side and then became bilateral, probably also affecting the diaphragm, and then followed by similar movements of the extremities. The twitchings were often accompanied by a general motor restlessness, which might develop into severe chorea. The patients found the twitching very troublesome and often painful. A moderate degree of fever was the rule, but the temperature was sometimes not raised at all. The general condition became rapidly worse, and most of the deaths in this year's epidemic occurred in this stage, which might last from several days to four weeks. The third or *lethargic* *stage* was marked by the appearance of bulbar phenomena and the subsidence of the signs of motor and sensory irritation, which were replaced by increasing somnolence. Death might also occur at this stage, but as a rule the second was the most dangerous. The lethargic stage was followed by a very protracted stage of convalescence, which might last for weeks, during which the patients complained of rheumatic pain, constant headache, dizziness, and fatigue. Occasionally slight relapses might occur at this stage in the form of isolated muscular twitchings or peripheral facial palsies, showing that the virus was very slow in being eliminated. In this connexion it is interesting to note that Jeanselme found the appearance of chorea and myoclonus following a lethargic stage accompanied by an increase in the cerebrospinal lymphocytosis, which he interpreted as indicating a fresh localization of the pathogenic agent.

Many other writers, such as Achard (2), Ascoli, Gerstmann, Sabatini, dwell on the great variety of the clinical symptoms in this disease. According to Achard (2) the principal symptom, somnolence, may show several degrees, ranging from slight drowsiness to coma. The psychical disturbance may be manifested by symptoms of depression or excitement. The ocular palsies are sometimes absent or very slight and transient. Other cranial nerves may be affected, and also the limbs. The paralysis may be accompanied or replaced by spasms. The general symptoms are equally variable. Some cases have a very high temperature, and others no fever at all. The febrile condition may precede the somnolence for ten days or more, or, on the other hand, the fever may outlast the somnolence.

Gerstmann enumerates the following varieties of encephalitis: *E. lethargica*, *E. choreatica*, *E. psychotica*, and *E. myoclonica*, so named according to the predominance of certain symptoms. He admits that it is exceptional to find an isolated clinical type. As a rule the symptoms are combined in various ways. Thus in some cases there is at first a condition of excitement accompanied by severe chorea which subsides in a few days and is succeeded by increasing lethargy, ocular disturbance, and muscular weakness. In other cases, after violent neuralgic pains, a psychosis becomes the prominent feature and is followed by muscular twitchings.

Bassoe states that since his previous paper (vide *Medical Science*, 1919, **1**, 89) he has become convinced that the same unknown virus produces clinical forms in which lethargy and other common symptoms of the characteristic lethargic forms are lacking. The similarity in morbid anatomy, the existence of transitional forms, and the occurrence of all these forms in the same community at the same time, show that one is dealing with the same disease. Several of his cases presented symptoms of a general infection suggestive of typhoid, acute miliary tuberculosis, and other acute infectious diseases. In other cases verified *post mortem* resemblance to acute chorea was marked. He also describes a meningo-radicular type characterized by irritation or paralysis referable to the spinal or cranial nerve roots.

The prevalence of myoclonic movements principally affecting the abdominal muscles, but also involving the limbs, has been emphasized by other writers in various countries as a distinguishing feature of the epidemic prevalent in the beginning of 1920, notably by Sicard and Kudelski of Paris, Gallavardin and Devic of Lyons, Creyx of Bordeaux, Ascoli, Sabatini, Tunola, and Boveri (1) in Italy, Stiefler, Dimitz (1, 2), Gerstmann and Grosz in Austria, Dumolard and Aubry, and Ardin-Deltheil and Raynaud (2) in Algiers, and Climenko and Reilly in New York. Sicard and Kudelski were inclined to regard 'myoclonic encephalitis' as distinct from lethargic encephalitis, owing to the absence of lethargy and ocular symptoms. Transitional forms, however, were soon reported in which a neuralgic or myoclonic stage was succeeded by a lethargic stage (Benard and Boissart), or, on the other hand, patients who had recovered from lethargic encephalitis developed myoclonic movements (Jeanselme), and in another group somnolence and ptosis were associated with myoclonus and delirium (Roger and Aymès).

In some cases Massari found the spasm of the abdominal muscles and abdominal pain so pronounced, and the other symptoms so much in abeyance, that the condition simulated a surgical disease such as appendicitis or intestinal obstruction.

A remarkable case of progressive ascending myoclonus in a man aged 19 is reported by Carnot and Gardin. The myoclonus started in the lower limbs, and invaded the abdomen causing paralysis of the bladder, then the upper limbs, and finally the face. Death took place a few days later. The necropsy showed gross lesions of the nerve cells in the cortex and medulla and extensive thrombosis of the meningeal veins extending over a large area of the spinal cord.

Claude (1) records three cases of a myotonic form of lethargic encephalitis in which the patients showed changes of muscular tonus independently of involvement of the pyramidal system. In two cases the physiognomy was absolutely expressionless, although somnolence was not a pronounced feature. An attempt to move the limbs was met by a marked rigidity of the muscles. One of the patients resembled a case of paralysis agitans, owing to his mask-like expression, muscular rigidity, and tremor of the hands. The resemblance of some of the cases to paralysis agitans is also emphasized by Sicard and Bollack, who regard this as favouring Brissaud's view that the lesions of paralysis agitans are situated in the *locus niger*, which is the principal site of the lesions in lethargic encephalitis.

The occurrence of incomplete forms (*formes frustes*) is regarded by Economo (1) as one of the characteristic features of this year's epidemic. They appear as nuclear forms with involvement of several cranial nerves, or as peripheral ocular or facial palsies, or as neuralgia, deafness, &c. Instances of these forms are given by Sicard and by Sabrazès and Massias (1). Epidemics of hiccough occurring simultaneously with those of lethargic encephalitis have been reported by several observers in various parts of the world, e.g. by Dufour and Benard in Paris, Gotti in Ravenna, and Boyd in Winnipeg. They may, as Benard points out, be regarded as incomplete forms of the myoclonic type of lethargic encephalitis. Examples of ambulatory forms in which the symptoms are very mild have been described by Sicard, Janet, Ramond, Flexner, Abbruzzetti, and Falcone, who emphasize their epidemiological importance.

The **ocular symptoms** of lethargic encephalitis are discussed by Morax and Bollack who summarize them as follows: bilateral incomplete ptosis, atypical diplopia, bilateral and symmetrical involvement of the vertical movements of the eyeball, inequality of the pupils, and paralysis of accommodation. The duration of the symptoms varies. Whereas ptosis and strabismus are only transient, involvement of the movements of the eyeball may last several weeks either as true paralysis or as paresis manifested by nystagmiform jerks. Disturbance of accommodation may last several months in lethargic encephalitis, in contrast with diphtheria, in which it does not last longer than a month or six weeks.

Two cases of more or less complete amaurosis accompanied by some impairment of hearing are reported by Clovis Vincent.

Guillain investigated the condition of the **reflexes** in six cases. In two which recovered both the tendon and cutaneous reflexes remained normal. In three the tendon reflexes in the upper and lower limbs were abolished, and in one case some of the tendon reflexes were preserved and others abolished. The cutaneous reflexes were preserved in all the cases. Guillain points out that the loss of the tendon reflexes in some cases of lethargic encephalitis with preservation of the cutaneous reflexes indicates a diffuse involvement of the neural axis, the lesions not being confined to the region of the medulla pons and cerebral peduncles. He regards the early loss of the reflexes as possessing a prognostic value, as the four cases in which the reflexes were abolished proved fatal, whereas the cases in which they remained normal recovered.

Gabbi found the oculo-cardiac reflex exaggerated in lethargic encephalitis and attributed this to hyperexcitability of the vagus centres in the medulla.

According to Lhermitte, Babinski's sign, Oppenheim's sign, and Monakow's sign (elevation of the inner border of the foot on stimulation of the sole) are fairly frequent in this disease.

Sequelae. Claude (2) found that persons who had had an attack of lethargic encephalitis might suffer from asthenia and be unfit to follow their ordinary occupation for a long time after apparent recovery, or have a recrudescence of certain symptoms such as paresis, choreiform movements, or visual disturbances. These sequels were readily explained by the vascular and perivascular lesions characteristic of the disease.

Encephalitis lethargica in pregnancy. According to Schulze, of San Francisco, the disease is much commoner in the male than in the female sex. Of 189 cases, collected by her from English and American reports, only 67 occurred in women and girls, and of these only 33 were women of child-bearing age. On the other hand, the mortality is considerably higher in women than in men. Of 122 men, 72 recovered, 23 died, and in 27 the outcome was not determined at the time of the report. Of the 67 women, 27 recovered, 24 died, and in 16 the result was not yet known. The mortality in pregnant women was particularly high. Of the eight reported cases, including that of Schulze, one recovered, four died, and in two the outcome was not reported.

Encephalitis lethargica and influenza. Economo (2) brings forward the following arguments against regarding encephalitis lethargica as one of the manifestations of influenza: (1) When the small epidemic of lethargic encephalitis occurred in Vienna at the end of 1916 and beginning of 1917 there was no epidemic of influenza in Vienna or Europe generally, and it was not until 20 months afterwards that influenza appeared in Vienna in epidemic form. (2) During the epidemic of influenza which began in Vienna in July 1918 no case of encephalitis lethargica occurred in any of its three waves, and it was only after the epidemic had subsided—that is, in the spring of 1919—that some cases of encephalitis lethargica were seen again in Vienna. In other towns also in which encephalitis lethargica occurred the outbreaks were distinct from those of influenza. (3) The morbid anatomy of lethargic encephalitis is quite distinct from that of influenzal encephalitis.

(4) The clinical picture of lethargic encephalitis is also different from that of the cerebral manifestations of influenza. Economo comes to the conclusion that lethargic encephalitis is a sporadic disease which may appear in epidemic form, and that epidemics of it may occur without any pre-existent or concurrent epidemic of influenza. Even in those cases in which it arises simultaneously with an epidemic of influenza it bears no causal relation to it, either in intensity or extent, but constitutes an entirely independent epidemic.

Page is inclined to the view that lethargic encephalitis is not an independent disease, but may be caused by the action of any toxin on the mesencephalon, such as that of influenza (Sainton) or syphilis (Lortat-Jacob and Hallez). He records two cases which occurred in tuberculous subjects, both of which survived their attack of encephalitis, the tuberculosis continuing its course when the lethargy disappeared.

Diagnosis. Boveri (2) emphasizes the following diagnostic features of lethargic encephalitis: (1) Bronchial or pulmonary localizations are never or hardly ever observed either at the beginning or during the course of the disease. Hypostatic pneumonia is merely a terminal phenomenon. This fact alone is sufficient to differentiate lethargic encephalitis from influenza. (2) The ocular and facial paralyses, both at the beginning and at the height of the disease, are transient, incomplete, dissociated, and variable. (3) The eye-muscle which is the first to be involved and which is paralysed longest is the ciliary muscle. (4) Retention of urine occurs early and is not accompanied by other sphincter disturbances. (5) Meningeal reactions in lethargic encephalitis are slight, both as regards increase in albumin and leucocytosis.

Differential diagnosis. This subject is discussed by Lhermitte and Blum, whose views may be summarized as follows: *Cerebrospinal meningitis*, with which encephalitis may be confused, is distinguished by the results of lumbar puncture. *Tuberculous meningitis*, a somnolent form of which occurs in the infant, is characterized by a dissociation of the pulse and temperature and irregularity of the pulse, which are absent in encephalitis. There is, moreover, an abundant cerebrospinal lymphocytosis which shows no tendency to decrease in the course of the disease. The *polioencephalitis superior haemorrhagica* of Wernicke affects alcoholics almost exclusively, is accompanied by very active delirium and severe lesions of the fundus, and fever is entirely absent. *Syphilis of the mesencephalon* is distinguished by the absence of fever, a positive Wassermann reaction, and diffusion of the lesions throughout the mid-brain. In *influenzal encephalitis* oedema is the principal lesion in the brain, dilatation of the vessels is far from being so pronounced as in encephalitis lethargica, and infiltration of the perivascular sheaths is absent. *Sleeping sickness* due to the *Trypanosoma gambiense* is differentiated by finding the pathogenic organism in the blood, cerebrospinal fluid, and glands. *The bulbar and pontine forms of Heine-Medin's diseases* are distinguished from encephalitis lethargica, which is most frequent in winter, by occurring in summer. Moreover, in infantile paralysis, the palsies are more generalized and accompanied by more marked changes in the cerebrospinal fluid. Complete restoration of function is less usual than in encephalitis, but the mortality is not so high.

According to Harvier and Levaditi lethargic encephalitis can be differentiated from poliomyelitis both histologically and experimentally. Poliomyelitis is accompanied by inflammatory lesions and neuronophagia, which are absent in lethargic encephalitis. Moreover, the monkey is not so sensitive to the virus of encephalitis as it is to that of poliomyelitis, as was shown by the writers' failure to transmit the disease to a Macaque monkey as well as to a rabbit. They suggest that the only resemblance between the two diseases is an epidemiological one, viz. the existence of abortive forms which are responsible for the diffusion of the disease in both cases.

Baudouin and Lantuéjoul report a case to show that a symptom-complex due to *cerebral softening* may simulate lethargic encephalitis. Their patient was a woman aged 57 whose symptoms were persistent somnolence, inequality of the pupils, strabismus, and loss of the light reflex. The cerebrospinal fluid showed an abundant polymorphonuclear leucocytosis. At the autopsy extensive softening of the right cerebral hemisphere was found.

Prognosis. Both Economo (3) and Netter (5), the chief authorities on this disease, are agreed as to its gravity. Economo estimates the mortality at about 40 per cent., and Netter states that apart from the abortive and ambulant cases about one-third of the patients succumb. The gravity of the disease he shows is due to several reasons, viz. involvement of the respiratory and circulatory centres in the medulla, paralysis of the ninth and tenth cranial nerves giving rise to pneumonia, and wasting and bedsores in chronic cases.

The bad effect of pregnancy on the course of the disease is exemplified by Netter (4) and Schulze.

While the prognosis is good as regards the ocular palsies, which clear up entirely, even if they last for months, Economo (3) points out that the outlook is less favourable in the case of choreo-athetotic movements and impairment of the mental faculties.

Prophylaxis. Flexner states that every effort should be made to determine the existence of and to detect and control the ambulant or abortive cases, as they may be more significant than the frankly lethargic and paralytic ones from the public health point of view. Since the nasopharyngeal secretions have become suspected of harbouring the morbid agent, adequate measures of controlling the distribution of these secretions should be carried out.

Treatment. In estimating the effects of treatment in lethargic encephalitis it is well to bear in mind Economo's (3) statement that it is very difficult to judge of the effect of therapeutic measures in a disease which has such an irregular course and is often cured spontaneously.

Barker, Cross, and Irwin found that lumbar puncture done for diagnostic reasons relieved the symptoms so markedly in several instances that it was repeated at intervals as a therapeutic measure. Immediate improvement following lumbar puncture is also reported by Spät.

Netter (4) recommends treatment by fixation abscess in all severe cases, and suggests that the good effects so obtained are due to the injection stimulating the organs in which the principles of defence are prepared. In a subsequent paper (5) he advises that fixation abscesses should be employed not only in severe cases but in every case, as soon as the diagnosis is established. Vincent is also in favour of this method.

Injection of convalescents' serum is advocated by Sabrazès and Massias (2) but is deprecated by Netter (4) on the ground that the existence of neutralizing principles in the convalescents' serum has not been demonstrated as in the case of poliomyelitis, whereas the presence of aggressins favouring infection is possible.

Favourable results have been reported following the injection of horse serum (Bellavitis), polyvalent influenza serum (Fendel), and antitetanic serum (Laubie).

As regards drugs, utropin internally is recommended by Netter (4) and Lhermitte as being the most active disinfectant of the cerebrospinal fluid. Netter also used jaborandi or pilocarpin so as to further the elimination of the virus by the saliva, and gives adrenalin at the same time to counteract the depressing action of these drugs upon the heart and also for the asthenia which is so common in these cases. Good results were obtained by Stephen and Bulchandani from the intravenous injection of salvarsan in cases in which utropin was of no benefit. Netter (4), on the other hand, has seen a case in which injection of neosalvarsan had a bad effect.

In maniacal attacks and in cases with choreiform movements in which all narcotics failed Spät found that hypnotism had an immediate sedative effect.

Maggiore, of Palermo, has treated nine cases (seven children and two adults) with intravenous injections of sensitized vaccines prepared from young cultures of Pfeiffer's bacillus. The number of injections varied from three to four and there was an interval of one or two days between each injection. The treatment appeared to have a favourable influence on the somnolence, ocular palsies, and general condition.

Crofton, of Dublin, also reports four cases in adults who rapidly improved after subcutaneous injection of pure influenza antigen.

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INFLUENZA

Histological. According to Rondopoulo, of Athens, the first epidemic of influenza on record is that described by Hippocrates in the sixth book of the *Epidemics,* which appeared at the end of November 426 B. C. at Perinthus in Thrace. The description of the symptoms is similar to that given by Huxham of the epidemic of 1733. Cough was the predominating symptom, and was accompanied by sore throat, pains in the thighs and legs, shivering, coryza, laryngitis, tonsillitis, bronchitis, and broncho-pneumonia, lassitude and weakness of the limbs. Mention is also made of otitis and renal pain. Apparently the epidemic was much more fatal in men than in women, only a small number of whom developed broncho-pneumonia.

Epidemiology. Edelmann, of the Wilhelmina Hospital in Vienna, emphasizes the enormous mortality of the present pandemic which forms a striking contrast in this respect with the epidemic of the nineties, and quotes the following sentences from Leichtenstern : 'an enormous morbidity associated with an extremely low relative mortality is one of the most striking epidemiological features of pandemic influenza. Expressions such as *vix unus evasit, nemini pepercit, correpti sunt fere omnes*, were constantly met with in the old writers, together with the statement that, apart from old men, weakly individuals, and phthisical patients, practically no one died of the disease'. Edelmann suggests that the present pandemic may be identified with the 'black death' of former times, the infection being the same as in the pandemic of 1890, but the *genius epidemicus* different.

A similar occurrence is frequently seen in the case of the acute exanthemata, especially scarlet fever.

An epidemic of considerable severity but short duration among the Lapps in the winter of 1918–19 is reported by Macklin, late surgeon to the Imperial Trans-Antarctic Expedition. All the sick cases as they occurred were thrust into bug-infested single-room huts and left there unattended until they died or recovered. About 50 per cent. of all cases died. The chief complication was broncho-pneumonia, from which there were practically no recoveries.

According to Cadbury, three definite epidemics of influenza appeared in Canton during the spring, summer, and winter of 1918, at the same time as the disease appeared in Europe and America. The spring epidemic was mild, the fever lasting only four days at most. The second and third epidemics were more severe, cases of pneumonia developed, and the fever usually lasted four to five days. One attack of the disease appeared to convey immunity against subsequent attacks. Foreigners in Canton were rarely affected and had only slight attacks. The mortality was relatively low, the disease being much less malignant in Canton than in the United States.

Motzfeldt has made inquiries through the agents of the life insurance society 'Fram' about all the deaths from pneumonia among the insured in the period July 1, 1918–January 1, 1919. Altogether 247 answers were received. After certain deductions, there remained 233 families in which one or more deaths from pneumonia had occurred. In 59 families, with a total of 199 members, there was no other case of pneumonia or influenza than that of the person who died. In each of the remaining 174 families there were one or more cases of influenza in addition to the fatal case. Again, among these 174 families there were 58 in which two or more cases of pneumonia had occurred. Thus, in 25 per cent. of the 233 families multiple pneumonia was observed, and in 13 families there were in each 3 to 6 cases of pneumonia. Among the 174 families, in which one or more cases of influenza occurred in addition to the fatal case, there were 858 members all of whom had presumably been exposed to infection with pneumonia. Of these, 79, or 9 per cent. (the fatal cases not being included), had contracted pneumonia. Among these 174 families there were 409 members who had contracted influenza, and of these again 19 per cent. developed pneumonia. Thus, if the fatal cases of pneumonia be included, there was a total of 583 cases of influenza, 253 of which developed pneumonia. Motzfeldt points out that the significance of these figures is partially obscured by the want of reliable data with which to compare them. For the pneumonia morbidity in cases of influenza during the recent epidemic showed as wide a range as from 0·5 to 22 per cent. His observations suggest that in certain families the multiplicity of influenzal pneumonia was very significant.

In an article on the influence of sex at different ages upon the severity of influenza, Apert and Flipo state that, contrary to the general rule in infectious diseases in which the influence of sex is nil, the influenza of 1918–19 was a much more fatal disease in the female than in the male sex, not only during the period of active sexual life, but from infancy upwards. On the other hand, the statistics for the city of Paris in the epidemic of 1889–90 showed that there was a greater mortality in the male sex.

In his Paris thesis on influenza at Bourges, Jacquet states that among 816 influenza patients who were in the hospitals at Bourges between

August 1 and October 31, 1918, there were 161 deaths, or a mortality of 19 per cent. The most fatal period of the epidemic was the first ten days of October, when the mortality was 24 per cent. This high mortality was due to the fact that out of 583 cases admitted to one hospital between August 15 and November 15, 360, or 63 per cent., had complications.

Bacteriology. In a paper based on his experience of the influenza epidemic in the hospital ship *Agadir* at Scapa Flow, from October 1918 to March 1919, Dudley states that the only constant factor in all the cases was the presence of *B. influenzae* in the patients' discharges during the febrile period of the disease. The organism was always found in cultures from the naso-pharynx if a suitable medium was used.

Morbid anatomy. According to Symmers, Dinnerstein, and Frost, of the Bellevue Hospital, New York, the first recurrent epidemic of influenza in New York in 1919 presented the following anatomical variations from the pandemic disease of 1918: (*a*) in the form of frequent and widespread inflammation of the pleura characterized by semipurulent and purulent exudates occurring in immediate association with pneumonic changes, (*b*) multiple small pleural or subpleural abscesses, (*c*) purulent infiltration of the interlobular and interlobar pleura, (*a*) solitary, or more often multiple, discrete or confluent intrapulmonary abscesses. In the pandemic of 1918, involvement of the pleura was conspicuously rare, whereas in the recurrent epidemic it occurred in 60 per cent., and in 40 per cent. purulent or semipurulent effusions were present. In the 1918 epidemic intrapulmonary abscesses were virtually unknown accompaniments of the pneumonic process. In the recurrent epidemic they were found in 35 per cent. of all cases. Sequelae might be expected in the form of (*a*) organization of the inflamed pleura with partial or complete obliteration of the cavity and interference with the excursions of the corresponding lung, (*b*) delayed, diffuse, or sacculated pleural or interlobar empyema, (*c*) fibrosis of the lung following organization of exudate in the interlobar or interlobular septum of the pleura, (*d*) gangrene of the lung and bronchiectatic cavities following secondary changes in intrapulmonary abscesses. In the 1918 epidemic pneumonia was virtually constant, both as regards incidence and conformity to type. In the recurrent disease it was relatively infrequent and the anatomical vagaries in the distribution and structure of the lesions were extremely frequent. In the pandemic of 1918, acute degenerative changes in the heart-muscle, liver, and kidneys were neither frequent nor intense. In the recurrent disease, on the other hand, they were both common and severe. In the pandemic, the blood-cultures were almost invariably sterile; in the epidemic, streptococcal septicaemia occurred in about 10 per cent. of all pneumonias.

Blood. According to Eschalier the most remarkable change in the leucocyte formula in epidemic influenza is the appearance of myelocytes. He found that myelocythaemia was a constant phenomenon, occurring in mild as well as in severe and complicated cases and within the first few days of the disease. Its diagnostic value is therefore considerable, especially in distinguishing influenza from febrile gastric derangement and typhoid fever. It does not possess any prognostic significance.

Montgomery and Dunham made blood studies in 30 cases of influenza in children aged from birth up to 12 years, and came to the following conclusions: (1) The tendency in uncomplicated influenza in infants and children is towards a leucopenia rather than a leucocytosis. (2) There is a tendency towards a slight leucocytosis in cases complicated by pneumonia. (3) In all the fatal pneumonia cases in their series the leucocyte counts were under 10,000. (4) The prognosis in general was better in pneumonia cases which showed leucocytosis. (5) Differential counts showed (*a*) a tremendous variation in the differential formula, (*b*) nothing sufficiently constant to be of clinical aid in diagnosis or prognosis.

Symptomatology. According to Coskinas, of Athens, who records 19 cases among soldiers aged 20 to 22, influenzal pulmonary lesions such as congestion, broncho-pneumonia, &c., are frequently accompanied by very small **aseptic pleural effusions**, which are sero-haemorrhagic, sero-fibrinous or less often puriform in character. The effusion may be transitory or of longer duration, occurring as a rule within the first few days of the disease or more rarely at a later stage. In a certain proportion of cases, which in the writer's experience did not exceed 13 per cent., the fluid undergoes a septic change. Aseptic pleural effusion in influenza may occur simultaneously with encysted or interlobar empyema. The cytological formula varies considerably both quantitatively and qualitatively.

Minet and Legrand record six cases of a **cardiac form of influenza** which they consider should be added to the classical forms of pulmonary, gastro-intestinal, and nervous influenza. A great variety of symptoms may be observed according as the whole or part of the heart is affected. Thus cardiac influenza may be manifested by endocarditis, pericarditis, with or without effusion, myocarditis, or nervous symptoms such as tachycardia, bradycardia, arrhythmia, and cardiac neuralgia. This form of influenza has no preference for either sex or for any special age, cardio-bulbar symptoms having been observed alike in infancy and in old age. Most of the cases, however, occurred between 20 and 45. Hearts affected by previous infections are more liable to be attacked than healthy ones. The influenzal virus may rouse old lesions into activity, create fresh lesions, or destroy the cardiac equilibrium by affecting the nervous system. Bacteriological examination has sometimes shown the presence of agents of secondary infection such as streptococci, pneumococci, or *B. influenzae*, but often no micro-organisms have been found, and in such cases the lesions are to be explained by the action of a filterable virus or by a toxin. The prognosis is usually grave, and a fatal issue is frequent, especially when there is an organic lesion of the heart. Sudden death is not uncommon, and complications such as embolism, pyaemia, cardiac failure, and collapse may occur.

According to Le Maux, who has collected 10 examples, 4 of which are original, endocarditis is a rare complication of influenza and appears to be due to the micro-organisms of secondary infection so frequently found in the blood of influenza patients, viz. pneumococci and streptococci. The pre-existence of old valvular lesions appears to be an almost indispensable factor for its development. The lesions found at the autopsy are those of vegetative endocarditis; ulcerative lesions appear to be rare. As a rule the vegetations are situated on the mitral valve and at the aortic orifice; in rare instances they are found in the right heart.

A fatal case of embolic gangrene of the right upper limb due to endocarditis is reported by Di Giuseppe.

Durand-Vaugaron describes a mild form of **haemorrhagic influenza** characterized by blood-stained expectoration followed by slight and transient haematemesis, or merely by occult intestinal haemorrhage which can only be detected by laboratory methods. As the general symptoms rapidly improve after these haemorrhages, the writer regards them not as the result of mere vascular dilatations due to vasomotor paralysis, but as an active mode of defence of the organism, which is trying to rid itself of limited infective foci. The disadvantage of this process is that it creates areas of congestion and superficial necrosis which are liable to give rise to secondary infection.

Prado, of São Paulo, draws attention to the late development of a mild form of intestinal haemorrhage in persons who have had a gastro-intestinal form of influenza. The blood is discharged either pure or as a black foetid mass, its evacuation being accompanied with vertigo, enteralgia, pallor, and shivering.

Thomson and Macauley, of Belfast, record four cases of post-influenzal **nephritis** in the same family, the patients being children aged from 4 to 13, in whom all other causes of nephritis could be excluded. In a review of the recent literature they show that the importance of nephritis as a complication of influenza is clearly recognized. Their conclusions are as follows:—(1) Nephritis is a more frequent complication of influenza than is commonly thought. (2) The virus of influenza may affect the kidneys in various ways: (*a*) by producing a temporary albuminuria as seen in many other acute infectious fevers; (*b*) by causing an acute nephritis during the course of the disease, especially if respiratory symptoms are present; (*c*) in convalescence, as in scarlet fever: (*d*) a dormant or latent nephritis may be lighted up. (3) Nephritis may follow even mild attacks of influenza. (4) Nephritis occurring during the course of influenza may be masked by the respiratory symptoms and only careful routine examination of the urine may demonstrate its presence. (5) The urine should be carefully tested not only in disease but also in convalescence. (6) The frequency and severity of the complication vary in different parts of the world and in different epidemics. (7) In the next few years a higher percentage of albuminuria may be expected.

Ordway reports 31 cases illustrating the **neurological sequelae** of influenza which were observed in the Boston City Hospital Neurological Out-patient Department from July 1918 to July 1919, and classifies them as follows:—I. Exhaustion group (11 cases): 1. Debility or fatigue cases. 2. Psychoneuroses of a neurasthenic or psychasthenic type. II. Neuroses (7 cases): 1. Occupational type (1 case). 2. Chorea (6 cases). III. Neuritis (2 cases): 1. Double ulnar neuritis. 2. Multiple neuritis. IV. Encephalitis (2 cases). V. Hemiplegia (4 cases). VI. Undetermined relationship (5 cases): 1. Transverse myelitis (2 cases). 2. Paralysis agitans (1 case). 3. Progressive muscular atrophy (1 case). 4. Post-influenzal athetosis (1 case). A remarkable feature of the cases was the comparatively good recovery in a comparatively short space of time. Ordway concludes that even extreme organic involvement of the central nervous system following influenza has a better prognosis in the majority of cases than similar conditions unassociated with this disease.

Porot and Sengès record three cases of *facial paralysis* in soldiers in connexion with influenza. In two the complication occurred during the acute stage and was of short duration; in the third it developed a week after the temperature became normal, but had not entirely disappeared eight months after the onset. As regards predisposing causes one patient had had signs of tuberculosis the year before and some pain in the ear, the second had had actual otorrhoea two years previously, but on the opposite side to the facial paralysis, and the Wassermann reaction was positive in the cerebrospinal fluid, though there was no other sign of syphilis. The third patient was a neuropathic subject, so that all the cases might be regarded as having a diminished general or local nervous resistance. The complication, however, was mainly due to an extension of the nasopharyngeal catarrh to the facial nerve via the Eustachian tube. Facial paralysis may thus be regarded as a local complication of influenza, which explains why it is more frequently met with than other affections of the peripheral nerves.

Moreau, of Avignon, reports a case of *paralysis of the ilio-hypogastric and ilio-inguinal nerves* most marked on the left side following an attack of influenza complicated by bronchitis in a man aged 19. Electrical examination showed marked faradic hyperexcitability of the obliquus externus on each side, especially on the left; electrical treatment was applied without success.

Dubourg reports six fatal cases of *purulent pneumococcal meningitis* in influenza which occurred among soldiers belonging to the French Army of the East at Salonica. The relative frequency of purulent meningitis as a complication of influenza in the Army of the East as compared with its rarity in France is attributed by Dubourg to the large proportion of native soldiers in this army and to the preponderating rôle of the pneumococcus in the complications of influenza. The black races are peculiarly susceptible to pneumococcic infections (vide *Medical Supplement* 1918, **1**, 449 *a*), and of the six cases reported only one occurred in a Frenchman, and the others in negroes or natives of Madagascar. Post-mortem examination showed that the accessory sinuses and ears were always intact, so that the meningitis was due to septicaemia. In most of the cases the onset of the meningeal symptoms was very sudden and death was never later than four days after the appearance of the first signs. All treatment was unsuccessful. The best plan is to prevent the development of meningitis by antipneumococcal serum subcutaneously or intravenously in any severe case of pneumococcal infection, especially during an epidemic.

Riese, of Carlsruhe emphasizes the frequent *involvement of the sympathetic* in influenza which is shown by a tendency to sweating, not only in the acute stage but also in convalescence, cyanosis, low blood-pressure, waxy degeneration of the muscles, alopecia, coldness of the extremities, lability of the pulse, palpitation, and frequent occurrence of sudden death due to intoxication of the sympathetic centre in the third ventricle.

A fatal case of *thrombosis of the superior longitudinal sinus* in influenza complicated by broncho-pneumonia is reported by Szigeti in an adult. The symptoms were acute confusion followed by epileptiform attacks. The thrombosis extended from the cribriform plate in front to the sigmoid sinus behind on the right and on the left to the transverse sinus. No lesions were found in the accessory sinuses or ear.

Clark reports a case of influenza, complicated by pneumonia, in a boy aged 2 years, with an unimportant family and personal history, who, two weeks after recovery, began to have almost daily both *grand* and *petit mal* attacks and whose whole mental development ceased.

Fell, whose previous paper on **post-influenzal psychoses** has recently been abstracted (vide *Medical Science*, 1919, **1**, 144–5) points out that a psychosis first noticed after influenza may have been pre-existent and not be influenced in its course by the infection. On the other hand, influenza may alter the aspect and course of an existing psychosis by hastening it or adding new features. Influenza may also precipitate an impending psychosis, such as general paresis, or it may aggravate some organic condition, e. g. cardio-renal disease, and bring on the mental symptoms usual in that condition. Cases of manic-depressive psychosis showed a marked predisposition (defective heredity and a history of a prior attack) and a tendency to early recovery. The infective type of psychosis usually ran an even course, and improved with the physical condition and did not show a marked tendency to relapse. Dementia praecox cases might begin as such, or with distinctly manic-depressive features, or with confusion and disorientation. They ran a rather rapid course and quickly assumed a hebephrenic character.

Gordon discusses the mental disorders following influenza in a paper based on the study of 62 cases which developed at the end of the febrile stage, during the period of asthenia usually succeeding infectious diseases. The majority (44) showed a more or less pronounced confusional type of psychosis with or without hallucinations, the symptoms being particularly marked in those with a psychopathic history. In the remaining 18 cases the most conspicuous feature was amnesia of a pronounced character. In each group improvement in the mental condition coincided with improvement in the general physical state of health.

Clemente, of Madrid, records two cases of severe **suprarenal insufficiency** in influenzal broncho-pneumonia characterized by intense asthenia, very low blood-pressure, and algidity, in which rapid improvement followed administration of suprarenal extract.

The occurrence of manic-depressive psychosis following influenza is also attributed to suprarenal insufficiency by Rossi, of Montevideo, who records nine cases in patients aged from 18 to 45.

In this connexion it may be noted that Symmers, director of laboratories of the Bellevue and Allied Hospitals, New York, found intense injection of the suprarenals a common post-mortem lesion and sometimes associated with haemorrhagic extravasation into the substance of the gland, or even accompanied by thrombosis of the suprarenal veins.

Skin. Schranz records a case of fatal gas gangrene following injection of caffein in a woman, aged 21, who, like many of the previously recorded cases, was suffering from influenzal pneumonia (vide *Medical Science*, 1919–20, **1**, 146, 442–3).

All the erythemata observed by Jacquet in the influenza patients at Bourges during the epidemic of 1918 were of one type, viz. *erythema marginatum aberrans*, a form of rash most usually seen as a late serum eruption. None of the patients had had any serum or vaccine treatment or received any special drug.

According to Meyer and Lucke, who report seven cases, subcutaneous emphysema is an exceedingly rare complication of influenza. In about 3,000 cases of influenza pneumonia it occurred in only nine patients, or 0·3 per cent., and in a series of over 12,000 cases of influenza in only 0·07 per cent. It developed most frequently in the neck region. The writers regard previous explanations of the condition as unsatisfactory and as the result of their post-mortem observations believe that the bronchial air escapes into the loose peribronchial tissues, and, by passing along lines of least resistance, gains entrance to the mediastinum and thence along fascial planes to the subcutaneous tissues. In this way the pleural sacs are not involved, and this accounts for the infrequency of pneumothorax in this condition.

Surgical complications. According to Prader, who alludes to Schmieden's recent paper on this subject (vide *Medical Science*, 1919, **1**, 45) many writers regard the surgical forms of influenza as frequent, while others consider them to be rare with the exception of empyema. Prader records four cases each of suppurative parotitis, thyroiditis, paranephritis, and abscesses of the soft parts, as well as two cases of arthritis of the knee-joint. Prader remarks that suppurative parotitis, which may occur at any time in sporadic form, is unusually frequent in an influenza period, especially at the height of the epidemic. In like manner mastitis without obvious cause, though otherwise so rare, has several times been recorded as a complication of influenza (vide *Medical Science*, 1919, **1**, 146, 253; 1920, **2**, 118) and Prader himself has seen two such cases. Numerous cases of arthritis occur during an epidemic. Prader has seen four cases of acute synovitis with rarefying osteitis exactly like a gonorrhoeal joint affection, although no gonorrhoea was present.

In addition to numerous cases of influenza, complicated by empyema, perinephritic and osteomyelitic abscesses, mastoid suppuration and purulent arthritis which required operation, Blac y Fortacin reports a fatal case of generalized pneumococcal suppurative peritonitis in a boy aged 12, which developed on the fifth day of an attack of influenza. He also records several examples of the malignant course assumed by influenza in cases which had recently been operated on, death taking place within 24 hours of the onset.

According to Gobrecht appendicitis was not a very frequent complication of influenza in the epidemic of 1918–19. Though sometimes the two diseases may commence simultaneously, as a rule appendicitis does not appear till three or four days after the onset of influenza, when the symptoms are subsiding. The diagnosis of appendicitis during an attack of influenza should not be made hurriedly, as the symptoms may be due to an influenzal pneumonia. Owing to the dangers attending an operation during an epidemic of influenza (vide Faure, *Medical Science*, 1919, **1**, 250), one should not be in a hurry to operate. Drey, who regards epidemic influenza as an important factor in appendicitis, records five cases of post-influenzal appendicitis in persons who had no history of a previous attack, and has collected similar cases from the literature. As a general rule, immediate operation is not required, but appendicectomy *à froid* after convalescence is advisable.

Throat. In a communication to the Berlin Laryngological Society on January 16, Versé stated that during the last three weeks he had seen several cases of influenza complicated by extensive necrotic tonsillitis, pharyngitis, and laryngitis. The anatomical lesions resembled the infarct-like necrosis of the lungs and pleurae seen in the mixed streptococcic infections of the 1918–19 epidemic. The practical significance of these cases lay in their resemblance to diphtheria. The disease started with the ordinary symptoms of influenza, but one or two days before death dyspnoea set in more or less suddenly. The cause of death, however, was not asphyxia but cardiac failure caused by toxic damage to the heart.

Hessberg, of Essen, has collected from literature 63 cases of the **ocular sequelae** of influenza, viz. 5 of palpebral abscess, 22 of conjunctivitis, 18 of keratitis, 1 of iritis, 3 of optic neuritis or retinitis, 1 of metastatic ophthalmia, 1 of accessory sinus disease, and 12 of asthenopia. He found that affections of the cornea were particularly severe, but that the prognosis was relatively good, whereas affections of the uveal tract ran a decidedly more unfavourable course, and the tendency to haemorrhages and the occurrence of septic metastases imperilled the function of the organ in the highest degree. Of special importance was the involvement of the eyes in meningeal and cerebral complications as well as the early relief of optic neuritis by repeated lumbar puncture.

A case of metastatic panophthalmia of the right eye which developed on the seventh day of an attack of influenzal broncho-pneumonia is reported by Oñate. Complete recovery followed enucleation (vide *Medical Science*, 1919, **1**, 47).

In an article on **influenza and tuberculosis**, Roubier, of Lyons, distinguishes three groups of cases: (1) Cases of prolonged or complicated influenza simulating tuberculosis (influenzal pseudo-tuberculosis). (2) Cases of definite pulmonary tuberculosis occurring after influenza. (3) Cases of influenza developing in tuberculous patients. The first group may be subdivided into two classes, the first showing persistent bronchitis or pulmonary congestion at one apex, and the second consisting of other prolonged forms of influenza simulating tuberculosis. The resemblance may be very close, especially when there are changes in the general condition, marked asthenia and loss of flesh, persistent sweats and repeated slight rises of temperature. The diagnosis is made by radioscopy, examination of the sputum, and the evolution of the disease. In a prolonged influenzal affection of the apex, the changes in the X-ray picture do not correspond to the signs in the chest heard on auscultation, the apex being more or less transparent and showing neither the pronounced opacity nor mottling usually seen in cases of tuberculosis. The sputum, though profuse and purulent, does not show tubercle bacilli in spite of repeated examination. Lastly, the evolution of the disease is a help to diagnosis, as at the end of a few weeks the abnormal physical signs disappear and there are progressive improvement in the general condition, gain of weight, &c. The persistence of bronchitis or pulmonary congestion at the apex is attributed by Roubier to the irritation caused by old sclerotic lesions. A guarded prognosis should be given as to the future of such patients, as it is possible that they may develop phthisis later. In other cases of influenza simulating tuberculosis there may be signs of a cavity at the base, or a pneumonia in which the physical signs persist or are very slow in disappearing. As regards post-influenzal tuberculosis, Roubier states that among 91 cases sent to him with suspicious bronchitis as the sequel of influenza 12 patients, or 13·2 per cent., were found to have definite tuberculosis. Most of them had no hereditary or personal history of tuberculosis. The development of tuberculosis following influenza in patients without any history of lung disease has been proved clinically and has also been established by autopsies, which show recent tuberculous lesions in addition to the resolving lesions of influenza. As regards the development of influenza in tuberculous patients, in some cases influenza has no definite effect, and the two affections run their course independently of each other. In other cases the rôle of influenza is distinctly unfavourable, as its occurrence may be followed by a rapid extension of the tuberculous lesions and a fatal issue.

As the result of an inquiry in the tuberculosis departments of the

Paris hospitals and military units devoted to tuberculosis, Debré and Jacquet found as a general rule that these establishments were very little affected by the influenza epidemic. Thus two wards at the Laennec hospital occupied by 50 civilians with tuberculosis completely escaped. In four military wards with 105 beds only three patients were affected. In the female department, which contained 50 beds, there were nine cases. The low incidence of influenza among tuberculous patients was associated with a mild character of the attack, pulmonary complications being exceptional. The writers attribute the comparative rarity of influenza in tuberculosis and its mildness when it does occur to a refractory state of the tuberculous organism to influenzal infection.

Burnand, director of the Leysin Popular Sanatorium, discusses the action of influenza on pre-existing tuberculosis and comes to the following conclusions:—(1) A previous attack of tuberculosis does not confer any immunity to influenza. (2) In about 75 to 90 per cent. of cases of chronic tuberculosis in which influenza develops the acute disease runs its course as an intercurrent affection without having any effect on the evolution of the tuberculous lesions. (3) 15 to 25 per cent. of tuberculosis cases undergo a considerable re-activation of their tuberculous lesions as the result of an attack of influenza. This recrudescence, however, is generally mild and transient if it is properly treated, and acute tuberculosis with fatal termination as the sequel of influenza is a rare exception. (4) The recent epidemic of influenza does not seem to have rendered latent tuberculosis active in a large number of cases. Out of 150 cases in which tuberculosis was associated with influenza Burnand saw only eight definite instances of this kind. (5) It is the doctor's duty, however, to prevent the development of post-influenzal tuberculosis by ordering a change of climate or residence in a sanatorium immediately after convalescence in cases in which tuberculosis is suspected.

In a paper based on the study of 150 cases of pulmonary tuberculosis and 210 cases of influenza under treatment at the Sandhof Municipal Hospital, Frankfort, between December 1918 and July 1919, Amelung comes to the following conclusions: (1) The incidence of influenza among cases of pulmonary tuberculosis is slight. Only 15 of Amelung's tuberculosis patients contracted influenza. The course of the acute disease, especially in slight cases of pulmonary tuberculosis, is milder than in the non-tuberculous, as is shown by the fact that in the 15 cases, who were all in the first stage of pulmonary tuberculosis, the attack of influenza was not attended by any complications. None of the advanced cases contracted influenza. (2) Pulmonary tuberculosis may develop as a sequel of influenza in persons with previously healthy lungs and in such cases the association of the two infections has a relatively unfavourable prognosis, as was shown by the fact that of 14 cases 10 died.

Mackay, of the Mowat Sanatorium for tuberculosis, found that open-air treatment was an important factor in warding off influenza. Of 75 patients in the sanatorium, 20, or 27 per cent., contracted influenza. The progressive, the far advanced, and the active cases in general escaped, and only the inactive cases developed the disease.

As regards the effect of influenza on cases of artificial pneumothorax, which was recently discussed by Burnand (vide *Medical Science*, 1920, **2**, 234), Weill reports four cases of this kind, in each of which the influenza was complicated by pneumonia at the base on the opposite side to the pneumothorax. In two cases death took place rapidly with hyperpyrexia, asphyxia, and cyanosis, due to the pneumonic process rapidly invading the whole lung. In the other two the pneumonia remained limited to the lower lobe of the lung and the disease ran its course like a frank pneumonia, the crisis occurring on the seventh and tenth day respectively.

Influenza in infants. According to Reiche, who is director of an infants' home in Brunswick, influenza in the autumn of 1918 generally occurred in a milder form among infants than in adults. In subsequent endemics, however, the course of the disease was as severe as in adults, and in such cases treatment was practically useless. The value of breast-feeding is shown by the fact that none of the breast-fed children died and one even escaped being attacked. Of the four fatal cases three were subjects of the exudative diathesis and the fourth had chronic encephalitis. From his experience at the University Paediatric Clinic at Turin, Rollandini states that suspension of breast-feeding when the mother has developed influenza is of no advantage to the infant, for the following reasons: (1) Artificial feeding diminishes the resistance of the infant to contagion and does not render the disease less severe. (2) Suspension of breast-feeding in a sick woman is more likely to cause rapid and permanent cessation of the milk secretion than in health. (3) Sudden weaning promotes the development of diseases of nutrition. Rollandini has seen a large number of cases of acute gastro-enteritis, some of which were fatal, among children who had been suddenly weaned owing to the mothers contracting influenza. (4) Influenza is a disease which spreads with such rapidity that when once it has invaded a family it does not usually spare any one. Rollandini therefore concludes that it is the doctor's duty to encourage the continuation of breast-feeding during the mother's influenza, except in cases of very severe complications, but that all possible precautions should be taken to prevent contagion. The child should be left in the mother's room as short a time as possible. The mother should not speak to or kiss the child, should refrain from coughing, and, if possible, should keep a handkerchief over her mouth while the child is at the breast.

Immunity. Bie has attempted to ascertain the frequency with which influenza confers immunity after a first attack, his material consisting of 521 cases of influenza in adults discharged from hospital between January 1, 1919, and July 31, 1919. In all but 55 of these cases information was obtained as to previous infection. Of the remaining 466 patients, 71, or 15 per cent., stated that they had already suffered from an attack during the recent epidemic, four of them twice. Bie concludes that the general belief in the permanency of the immunity conferred by influenza is erroneous.

Diagnosis. The following differences between influenza and pneumonic plague are set forth by Broquet, who had an opportunity of studying the latter disease in Manchuria and China in 1911: (1) In all the cases of pneumonic plague *B. pestis* could be isolated from the blood or sputum, often in pure culture, whereas no one has ever found this organism in the blood or sputum of influenza cases. (2) Pneumonic plague is invariably fatal, the great majority of cases dying within two days. Influenza does not show a uniform degree of severity, but may occur in a mild as well as in a severe form. Although some cases run a severe course and kill the patient in two or three days, or even in a few hours, the disease as a rule lasts some time. (3) Pneumonic plague has been confined to a definite part of Asia, viz. Manchuria and Northern China, whereas influenza has a world-wide distribution. (4) The modes of contagion and methods of protection are well understood in a pneumonic plague. Contagion is conveyed from man to man in drops of saliva. With a good mask covering the whole face, the body protected by hermetic overalls and rubber gloves and boots, the healthy man can approach the severest case of pneumonic plague with impunity. In influenza, on the other hand, the mode of transmission cannot be established as long as the causal agent is unknown.

Prognosis. Bie has compiled a series of tables from a material of 1,653 hospital cases of influenza, for the most part complicated by pneumonia or bronchitis, with a view to showing by statistics the significance of heart disease, albuminuria, pulse-rate, temperature, and respiration in relation to the prognosis in influenzal pneumonia. Of the 55 patients whose pneumonia was complicated by heart disease, 31, or 56 per cent., died. The mortality among adult patients with pneumonia uncomplicated by chronic heart disease was only 21 per cent. Albuminuria as a complication was also shown to be of sinister omen: it occurred in 29 per cent. of the patients with pneumonia and only in 4 per cent. of the patients without pneumonia. The mortality of the patients with combined pneumonia and albuminuria was 35 per cent., that of the patients with pneumonia only was 12 per cent. No prognostic significance could be attached to the height of the temperature on admission, as judged by the subsequent fate of the patients; nor could the relation of the temperature in the morning to that of the previous evening be construed as a sign of prognostic significance. Of far greater importance in this respect were the pulse and respiration, particularly the latter. A pulse-rate of over 130 on admission was noted in five fatal cases and only in one terminating in recovery. It was noticed that the pulse-rate and temperature did not always coincide; one patient with a pulse of 60 had a temperature of 103·8°. Respiration of 40 or more proved to be ominous, whereas the prognosis was comparatively good when the respiration was 35 or less.

According to Toulze, who devotes his Paris thesis to the subject of fixation abscesses in the treatment of influenza, all writers are agreed in attributing considerable prognostic value to the method. When the abscess takes and a vigorous local reaction occurs, this is a good sign of recovery. On the other hand, when the abscess does not take, it is a grave sign indicating inability of the organism to furnish a reaction to infection. In 21 cases in which the abscess did not develop, 19 died and only two recovered. The formation of the abscess however has less prognostic value, five of the cases in which one developed proving fatal.

Prophylaxis. The results of inoculation against influenza in the home commands from 1918 to 1919 are summarized by Sir William Leishman as follows:

	Strength.	Incidence of attack.	Incidence of pulmonary complications.	Deaths.
Inoculated	15,624	14·1%	1·6%	0·12%
Non-inoculated	43,520	47·3%	13·3%	2·25%

Nearly one-half of the inoculated received only the first dose of the vaccine, i. e. one-third of the amount considered essential to effective protection. It is probable, therefore, that had all received the full dosage the protective results would have been still more evident. No bad effects were reported from the inoculations, and the reactions in the overwhelming majority were trivial or non-existent. The formula of the vaccine now employed in the army, and also by the Ministry of Health, contains *B. influenzae* 400 millions in place of 60 millions as previously, streptococci 80 millions and pneumococci 200 millions in 1 c.c.

Wynn uses a vaccine containing equal numbers of Pfeiffer's bacilli and various strains of pneumococci and streptococci recently isolated. He regards the following doses as sufficient: a first dose consisting of 100 millions of each organism and after one week 200 millions at first, but later increased to 200 and 400 millions. In several cases a third dose of 800 millions, and a fourth of 12,000 millions were given.

Treatment. In a paper on hospital hygiene and influenza, Lesage states that whereas the mortality from influenza among children of all ages nursed in a common ward is 22 per cent. (Netter), at the Hôpital Herold, where each child is in a separate cubicle, the mortality among 301 cases of influenza in children of all ages was 11·29 per cent., 14 of the 34 fatal cases dying within the first twenty-four hours. After this period the mortality sank to 6·96 per cent. The mortality was highest in the infant, viz. 23·52 per cent. and lowest between three and five years of age, when it was 7·46 per cent.

The intravenous injection of **hydrogen peroxide** for influenzal pneumonia is advocated by Oliver and Murphy, who used it in 25 cases with 13 recoveries and 12 deaths without gas embolism being produced. The anoxaemia was often markedly benefited and the toxaemia appeared to be overcome in many cases.

Toulze regards a **fixation abscess** as specially indicated in forms of influenza in which a severe infection predominates, and before the appearance of any visceral localization, especially of a pleuro-pulmonary nature. A pulmonary focus, however, is not an absolute contra-indication. The success of the method mainly depends upon its being employed early, and one should not wait until signs of profound intoxication have occurred. The technique is as follows: 1 or 2 c.c. of oil of turpentine is injected subcutaneously into the middle part of the outer surface of the thigh. If no reaction occurs at the end of a few days, the injection must be repeated. Incision should not be delayed too long, but should be performed on about the fifth or sixth day. The production of a fixation abscess is also recommended by Probst, of Berne, in all cases of severe influenza (vide also *Medical Science*, 1919, **1**, 52–3).

Serum therapy. Redden, who, in conjunction with McGuire, had previously reported on 151 cases of influenzal broncho-pneumonia treated by convalescent human serum (vide *Medical Science*, 1919, **1**, 53), now presents the results of similar treatment in 100 cases in private practice. The total number of deaths was 16, but excluding cases in which the serum was given too late in the disease, and also those who died of complications other than pneumonia, there were only three deaths. From his own observations and the reports of twelve other observers, Redden concludes that when the diagnosis is made early and the treatment correctly carried out, the course of the disease is decidedly shortened, the death-rate is at least reduced by half, and even by three-quarters in any large series in hospital practice.

Thirty-nine cases of influenzal pneumonia were treated by Friedemann with anti-influenzal pneumo-streptococcal serum. A not inconsiderable proportion of the cases failed to show any reaction, but in 14 the serum appeared to have a very favourable effect. Friedemann, however, as on a previous occasion (vide *Medical Supplement*, 1919, **2**, 76 *a*) is doubtful as to whether this beneficial effect is due to the specific action of the serum on the pneumococci or to the non-specific action of the horse-serum.

Vaccine therapy. Lochelongue describes the vaccine G of the Institut Pasteur, the composition of which was at first pneumococci 4.000 millions, streptococci 2,000 millions, and *B. influenzae* 2,000 millions. Subsequently its formula was changed to streptococci 5,000 millions and *B. influenzae* 5.000 millions. The vaccine proved absolutely harmless whatever the age of the patient, and the local reaction when it did occur was insignificant. The use of the vaccine was followed by a rapid and striking reduction in the number of organisms in the sputum. In most of the cases the fall of the temperature occurred suddenly after the fourth, and exceptionally after the third injection. The pneumonic form of influenza appeared to benefit most from the treatment.

Lavatelli, of Turin, has used Bruschettini's polyvalent vaccine, which contains various strains of streptococci and pneumococci, in 238 cases of influenza of all degrees of severity, with a total mortality of 1·2 per cent., whereas the average mortality among his cases before the use of the vaccine was 8 per cent. The injections were given in the gluteal region, less frequently in the abdomen, and in a few cases intravenously, in doses of 2 c.c. daily for two, four, or five days in succession.

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J. D. R.
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GONORRHOEA

Symptomatology. With a view to gaining a survey of the frequency and symptomatology of gonorrhoea of the rectum in women, Boas has systematically examined the rectum of every woman treated for gonorrhoea during the past 2½ years at the Frederiksberg Hospital, Copenhagen. The result of the examination was not regarded as positive unless gonococci, taking Gram's stain, were found. Every case of proctitis was examined by the rectoscope, and the motions every day for mucus, blood and pus. Gonorrhoea of the rectum was found in 14 out of 88 cases. A striking feature of these 14 cases was the lack of severe symptoms; only one patient complained of pain on defaecation, and only in three cases was the skin about the anus red. But in as many as 11 cases mucus and pus were found in the faeces, and in one case much blood. Boas notes as exceptionally interesting the fact that in two cases gonococci were found in the rectum at a stage when nothing abnormal could be found in the motions in spite of daily examinations. In both cases the gonococci disappeared after four weeks without treatment. This total absence of macroscopic signs of disease, and the spontaneous recovery have not been hitherto observed. Boas disagrees with the current view that gonorrhoea of the rectum usually runs a protracted course, passing into a subacute or chronic stage lasting for months. In ten of his cases the gonococci and the symptoms disappeared under treatment in two to four weeks. The remaining four cases took longer, but only in one of these did the gonococci persist for as long as four months. Only one case was complicated (abscess of the anus). The treatment adopted was irrigation, morning and evening, with a 1 in 3,000 solution of permanganate of potash at a temperature of 40° C. This was introduced through a Y-shaped tube, and successive quantities of the solution were drawn off after a stay of about 5 minutes in the rectum. Great importance was attached to the maintenance of the temperature of the solution, as the gonococcus is very susceptible to a temperature of 40° C. After the irrigation, an ichthyol pessary was inserted, and when a case proved refractory to this treatment it was supplemented by irrigation with a 2 per cent. solution of protargol. As gonorrhoea of the rectum often provokes no symptoms, and as its neglect may lead to reinfection of the genitals, Boas recommends the routine examination of the rectum in every case of gonorrhoea in women.

Prophylaxis. Castellani, having found that bile and bile salts prevent the growth of gonococci *in vitro*, tried a solution of **taurocholate of sodium**

in glycerine (2 to 4 grm. in 30 grm.) as a prophylactic measure against gonorrhoeal infection. A few drops of this fluid are placed in the urethra and also on the glans penis before coitus, and afterwards, after washing. Two experiments were made on the human subject: in the first, gonorrhoeal pus mixed with the taurocholate solution for three minutes was placed in the urethra; in the second, the taurocholate solution was applied first, then gonorrhoeal pus after an interval of 3 minutes; the subject then micturated, and injected more of the taurocholate solution. In neither case did infection occur. The advantages of this prophylactic are cheapness and absence of irritation.

Treatment. Belfield advocates **injection of collargol into the seminal vesicles** in cases of acute gonorrhoea. He holds that the vesicles are affected in more than half the cases of acute gonorrhoea; that acute gonorrhoeal vesiculitis usually receives only symptomatic treatment combined with vaccines, and when unresolved is responsible for many cases of gleet; that the vesicles are easily filled with a suitable solution by puncture of the vas; and that gonorrhoeal epididymitis is always an extension from the infected vesicles, and should be prevented by timely treatment of the latter. The technique is as follows: the vas is pressed against the lateral scrotal wall and fixed by two pairs of tenaculum forceps; the vas is then exposed through a small incision and punctured; a fine silkworm thread is inserted and a blunt hypodermic needle threaded over it; through this 10 c.c. of 1 in 25,000 solution of methylene blue is slowly injected; this causes desire for micturition, and if the dye appears in the urine the technique is correct; 20 c.c. of a 5 per cent. solution of collargol are then injected slowly, followed by 1 c.c. of water. The puncture in the vas is kept open for subsequent injections by a silkworm thread fixed in it. Collargol is used on account of its penetrating power, its liquefying action on semi-solid purulent masses, and its harmless effect on the vesicle. The urethra requires to be treated separately by the usual methods.

Goldstein claims good results from the combined administrations of **anti-gonococcal serum** and **polyvalent vaccines** in gonococcal septicaemia and metastatic gonorrhoea. The serum was given in doses of 10 to 15 c.c. on successive days up to a total of 50 c.c., the vaccines in doses of $\frac{1}{4}$ up to 4 billions. In severe cases the serum was injected intravenously. Occasionally, an anaphylactoid reaction occurred on the 8th or 10th day: this was controlled by 15 minim doses of 1 in 1,000 adrenalin solution every 4 or 5 hours, together with 1/500 to 1/100 grain of atropin. Goldstein, while recognizing the importance of examining the teeth, tonsils and sinuses for the cause of arthritis, remarks that patients sometimes have their teeth and tonsils removed for rheumatism due to foci of gonococci, the most common situations for which are the prostate or seminal vesicles in the male and the Fallopian tubes in the female.

Fraser and Duncan report their results from the **intravenous injection of vaccines** in gonorrhoeal rheumatism. The cessation of urethral discharge in gonorrhoeal patients infected with influenza led them to assume that a rise of temperature helps the tissues to counteract the action of microbes and their toxins. They mention the experiments of Rolly and Meltzer, Ludke, and others showing that heated animals were more resistant to bacterial infection and produced more bacteriolytic substances. They also mention the experiments of Petersen and Jobling, who injected animals intravenously with bacteria, kaolin, protein-split products and trypsin and found an increase of proteose and lipase in the serum. These workers obtained similar reactions in patients after intravenous injection of vaccines and proteoses, and improvement in certain infections, attributing the effect to the digestion of microbes and their toxins by ferments.

Fraser and Duncan report 15 cases of gonorrhoeal rheumatism, all of which were improved. They note that no benefit followed an injection that was unaccompanied by rise of temperature. The vaccines used included gonococcus vaccine in doses of 25 to 2,000 million, some combined with staphylococcus and diphtheria vaccines, and in some cases T.A.B. They regard the action of these vaccines as due to the production of specific antibodies by non-specific germ constituents, since the vaccines they used had been stored for some time and were probably detoxicated, and they suggest that a vaccine minus its endotoxin may be regarded as a non-specific proteose in a colloidal form.

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THE SURGICAL TREATMENT OF UNDESCENDED TESTICLE

It is necessary at the outset to exclude the condition which is only a slight variation from the normal, viz. the delayed descent of the testes. Galen distinguished the condition of a *kruptorchis* from that of *anachoresis lat: recessus*, the withdrawal of the testes into the abdominal cavity, such as occurs in some animals. Both the delayed descent and the withdrawal are seen in boys. French noted the experience of Armstrong as doctor to a public school; in half a dozen cases of delayed descent of both testes a normal descent of both had taken place within a year; only in one case one of the testicles passed into the perineum. In such cases there is no tendency to disease; there is an active cremaster which withdraws the testis, as well as a persistence of the muscular fibres belonging to the cremaster which are attached to the fundus of the scrotum, the *musculus descensus testiculi*, to which Hunter gave the name of gubernaculum or pilot. After the definite descent of the testis, the muscular fibres disappear and a ligament is formed, often called *ligamentum Hunteri*. But such testicles are not liable to disease, neither to torsion, nor to malignant disease. Active spermatogenesis commences in them about puberty and apparently determines their late descent.

A true cryptorchid has the testis detained by a definite pathological condition whether in the abdominal cavity, the inguinal canal, or in the groin outside the external ring. Whatever be the cause, there is an inflammatory fibrous thickening of peritoneum which is united to the cremaster fibres underneath as well as to the fibrous tissue amongst the pampiniform plexus of veins. On the other hand the vas deferens and its blood-vessels, also the spermatic artery is not involved. There is sometimes a thickening of the tunica albuginea and an increased formation of fibrous tissue between the tubules of the testis. However, in most of the cases the testis has an abundant supply of tubules in the resting stage before puberty. The cells of Sertoli and the interstitial cells are present, affording evidence of an active internal secretion of the testis. After the testis has been placed in the scrotum, spermatogenesis develops.

A retained testis is liable to complications; if its descent has been arrested in the inguinal region, it is there more or less fixed and therefore cannot be pushed aside as in the scrotum: but more importantly it is generally, although not always, complicated by hernia, the sac of which may be bilocular. Also if the testis has a pedunculated connexion, to use Pott's phrase, like a clapper within a bell, the mesorchium is liable to torsion. But the most important complication is that of the special liability of the retained testis to develop malignant disease, whether in the inguinal region or in the abdominal cavity. It is obvious that this is related to the causes of an inflammatory nature which have fixed it and prevented its descent. In confirmation of this is the absence of any report as to the development of malignant disease in a testis once it has been freed and placed in the scrotum. Coley in reporting on 334 cases in which retained testes had been placed in the scrotum, traced the later history of 185. The result was good; only in one case did sarcoma develop, and that so shortly after the testis had been placed in the scrotum that it was probable that the disease had already started.

It is of grave importance that retained testes tend to become malignant; the malignant disease has been always of such a virulent kind that the patients have died. The removal of a retained testis after it has become malignant has failed in nearly all cases to save the patient. It has turned out that either metastatic growths have already arisen, or the disease has soon recurred after the excision.

Attention was especially directed to the matter in 1907 by Osler. A man aged 36 had his right testis retained in the groin. It had been swelling for 18 months when it was excised and found to have become a myxosarcoma. Eighteen months later the patient presented retroperitoneal masses.

A man aged 29, a cryptorchid, had the abdomen distended by a tumour and free fluid. The retained right testis had rapidly developed into a sarcomatous mass and this was removed. But the disease soon recurred.

A man of 46, with only the right testis in the scrotum, had an inoperable abdominal tumour and ascites. A similar instance occurred in a man aged 45. Darby reported the case of a man aged at death 24. He had had a congenital left inguinal hernia, and the testis was absent from the scrotum and inguinal region; the penis was hypospadiac. An abdominal tumour was discovered $1\frac{3}{4}$ years before death, when it was found fixed to the spine and deemed inoperable.

Bulkley collected 57 cases of malignant disease in undescended testicles; 30 were on the right side and 24 on the left, two were bilateral, and in one the side was not noted. He saw a third bilateral case in a farmer aged 38, who was married but had had no children. His testes had been retained in the groin. At 30 he had an attack of mumps, when both testes swelled up and were very painful; after they had subsided, he had experienced no more trouble until two months before coming under observation. Then each testis had begun to swell and the enlargement was found to consist partly of sarcoma, partly of fluid in the tunica vaginalis. Both tumours were excised and the cord followed into the pelvis as far as possible. The right tunica vaginalis contained 750 c.cm. of fluid, the left less. Each testis was the seat of a large round-celled sarcoma.

In Tirmurti's case, a man of 35 had only been ill for two months before his death, which was due to metastatic growths spreading from a malignant right testis retained in the abdominal cavity. The primary growth was the size of a coco-nut and was found to be an instance of chorion epithelioma.

Huguet reported a case of embryonal carcinoma arising in the testis retained in the inguinal canal of a man aged 30. It had been enlarging for a year. Downes saw a similar case in a man aged 45.

These are instances of the general rule that when a retained testis is noted to be enlarging it is too late, owing to the very malignant character of the disease.

A quite exceptional case as regards malignancy was that described by Outland and Clendenning. A man aged 65 had had an abdominal tumour for 15 years, which had enlarged rapidly in the previous three years. Death followed exploration, when it was found that the left testis had become a large cyst with a fibrous wall. The wall was intimately adherent to the diaphragm, left kidney, tail of the pancreas, and spleen. No testicular substance or new growth was found in the wall. Apparently the cyst had developed in the original position of the embryonic testis.

This tendency to malignant degeneration appears to be absent in the cases of ectopia testes, which may be attributed to variations in development of the gubernaculum testis. The testis, whilst developing from the genital ridge at the back part of the abdominal cavity, becomes connected with the anterolateral abdominal wall by a ridge termed the inguinal crest. In this crest appears a slender band of unstriped muscle which comes to connect the skin of the scrotum through the inguinal canal with the body of the testis and the epididymis. At the same time there is developed the tunica vaginalis as a peritoneal sac which pushes its way through the inguinal canal into the scrotum. As it does so it carries with it loops of the internal oblique muscle to form the cremaster; the ascending portion of the loops are inserted into the spine and crest of the pubes and the sheath of the rectus abdominis. Some of these loops consisting of striped muscle fibres surround the unstriped fibres forming the core of the gubernaculum. At its lower end the gubernaculum has four tail-like endings, the scrotal being generally the dominant one. Exceptionally it is otherwise, and the tail ending in the perineum directs the descent of the testis; rarely an attachment to the skin overlying Scarpa's triangle causes the testis to be dragged out through the crural canal, when it is found superficially in

Scarpa's triangle. The pubic strand of the cremaster may draw the testis towards the middle line when it is found in front of the pubes at the root of the penis. In the female the corresponding structure becomes attached to the uterus and forms the ligament of the ovary; beyond this, between the uterus and the labium majus, it constitutes the round ligament. The pouch or peritoneum which accompanies the round ligament is analogous to the tunica vaginalis in the male. When the gubernaculum fails to become attached to the uterus the ovary is drawn down through the inguinal canal into the labium majus.

It is noteworthy in connexion with the operative treatment that the cremasteric branch of the deep epigastric artery supplies the remains of the gubernaculum, through which there is an anastomosis with the spermatic artery and with the artery of the vas deferens.

The commonest variety of ectopia is the perineal.

Loewe added to a collection of cases on this subject previously made by Guégan, making altogether 86 in number. In a boy of 12 the cord was traced over the external abdominal ring down to the testicle placed in the perineum 5 cm. in front of the anus and 2 cm. to the right of the median raphé. Attached to the lower pole of the testis was a strong fibrous band, the remains of the gubernaculum, which was inserted into the tunica dartos 2 cm. in front of the anus and 2 cm. from the middle line. This band was cut across and the testis put into the scrotum.

The following case illustrates what has been met with on other occasions, the dragging down of a loop of the vas deferens by the gubernaculum. A man aged 21 presented what at first sight appeared to be a left congenital hernia with a very atrophied testis. On more careful examination the supposed testis proved to be a loop of the vas deferens. On exposure through an incision a patent funicular process of the tunica vaginalis was traced up through a normal inguinal canal, but there was no hernia of the abdominal contents. In the wall of the sac was the vas deferens of normal size. Traced downwards, it was found to be sharply reflected and was then continued upwards as a tortuous tube formed by an unravelled epididymis about half the thickness of the vas. This ended in a testis lying just within the abdominal ring. The testis was rather more than half the size of the right, softer, and without a normal epididymis. At the angle made by the loop of the vas was attached a band of white fibrous tissue, about two inches in length, representing the gubernaculum testis. Its other end was continuous with the dartos, so that, as the band was drawn upwards, the scrotum at the point of the attachment followed and was drawn inwards.

The testis is usually protected from accidents by the sessile character of its mesorchium. As it develops from the genital ridge it is attached to the mesonephros by a fold of peritoneum, in which the spermatic vessels are formed by separation from those of the mesonephros. When the testis is not sessile or anchored by the remains of the gubernaculum to the bottom of the scrotum, it may hang free in the scrotum with its mesorchium as a peduncle. In the case of the two soldiers admitted to the Westminster Hospital for sudden and acute pain in the scrotum, torsion of a testis hanging free in the tunica vaginalis was found. In one case the condition was correctly diagnosed before operating because the testis was felt reversed with the epididymis directed forwards. In neither case could a definite history be obtained, as to how the torsion had occurred.

Torsion of a testis retained in the inguinal region has been frequently noted of late years. Langton in 1882, in a man aged 33, cut down upon a retained testis, turned out blood-clot, and found that a freely hanging testis had undergone torsion. The tunica vaginalis was drained, but the testis sloughed away in the course of the following month.

Operations for undescended testis. The principal reason for excising an undescended testicle is that malignant disease threatens to or has already supervened. Thus Pott, in the case of a middle-aged man, whose left testis had been retained in his groin, because it had enlarged during the previous two years, advised removal. Other advice opposing this, there was a delay of some months and when it was removed it had 'now become scirrhous'. Unfortunately, if the retained testis has already begun to give trouble, the excision may be too late. Thus in Arnott's case the patient died from facial erysipelas twelve days after the excision of a testis retained in the groin. On post-mortem examination a small malignant growth was found just within the internal ring and a large mass at the root of the mesentery. Cushing mentions with the foregoing a case under Storks who died of malignant disease in the abdomen fourteen months after the excision, and one under Fayrer who died from the same cause in twelve months.

There has accumulated evidence since then to show that any alteration in the retained testes in the direction of thickening of the tunica albuginea or hardening of the substance of the organ should be treated as evidence of imminent or actual malignant disease. To be more exact, a microscopic examination might be made of a small bit during the operation.

The placing of the retained testicle in the scrotum is stated by Curling to have been first performed by Koch of Munich in 1819. A man aged 26 had one testicle retained in the groin; on incising the tunica vaginalis an ounce of fluid escaped; the testis was of considerable size but soft, the cord convoluted and varicose. The testicle was then placed in a cavity prepared in the scrotum to receive it and secured by a suture to the septum, in order to prevent the gland being drawn up by the action of the cremaster muscle. The testicle showed a disposition to return to its former position and the cure proved tedious.

This is the particular variety of operation which has apparently been most often adopted.

Bevan of Chicago, in 1903, gave a more detailed account of freeing the testicle by dividing the peritoneum, the cremaster, and in part the pampiniform plexus, the procedure approximating to the operation commonly performed for varicocele.

Colez, of 334 cases in which he had generally followed Bevan's method and placed the testis in the scrotum without sutures, was able to trace the results in 185 cases. Only in a small number was the testis found at the bottom of the scrotum some years after the operation. Especially if atrophic, it had retracted to a mid-scrotal position or near to the external ring. Keetley in 1894, in order to counter the tendency to retraction, passed the testis through a button-hole incision made at the bottom of the scrotum and fixed the testis in a pocket made under the skin of the adjacent portion of the thigh. In one case the testis was held in the pocket for five months before being put back into the scrotum. The case was exhibited nine years later, after the boy had grown up; the testis had increased but remained smaller than the opposite one and was placed a little higher up.

A less elaborate method was described by Hahn in 1902: the testis is brought out through a button-hole at the bottom of the scrotum and fixed there by a single stitch. After four or five days it is covered with vascular granulations, when the boy is given gas and the testis pushed back just within the skin. This method of Hahn's has been systematically followed since. The advantages are that the testis becomes adherent at the bottom of the scrotum, where it is normally fixed by the remains of the gubernaculum. There it has the opportunity of getting a vascular connexion with the dartos and so an anastomosis with the spermatic artery and that of the vas deferens, which improves its nutrition and favours development. In bringing the testis out through a button-hole at the bottom of the scrotum, an opportunity is given for blood to escape. Blood-clot then does not collect in a blind pouch. Bilateral cases can be quickly done at one sitting.

Villemin, in 1899, proposed the method of passing the testes through the scrotal septum.

Philip Turner has recently followed the method in twelve instances; in one bilateral case the left testis was passed through the raphé of the scrotum to the right side, and five months later the right testis passed through to the left side of the scrotum. Five years later the result was good, both testes had increased in size.

The so-called 'necktie' operation, advocated by Milon of Paris, would seem to have the same objection as the application of a truss to keep the testis down. After putting the testis into the scrotum, Milon cut two strips from the aponeurosis of the external oblique on either side of the external abdominal ring: the strips were then tied round the cord. But like a truss this tie must compress the cord and favour atrophy of the testis rather than its development.

In the case of great difficulty, when the testis cannot be raised without dividing the cord, the method adopted by Philipowicz offers the opportunity of preserving the internal secretion of the testes. Failing to free the testis whilst still attached to the cord, he divided this last, leaving the testis connected to a vascular gubernaculum. The testis was then placed in the scrotum, supplied with blood through the deep epigastric artery, and it did not atrophy or slough.

Undue emphasis has been put upon the observation that a retained testis shows no signs of spermatogenesis. That is generally the case so long as it is retained, the gland continues in the stage existing before puberty. But experience of the operation shows that when the testis has been placed in the scrotum and has a sufficient vascular supply it increases in size, and with the onset of puberty develops spermatogenesis. Coley noted two cases of bilateral retained testes which were placed in the scrotum. Both men married and had children.

The success of the operative treatment clearly indicates that, however young the case, if hernia complicates a retained testis the operation should be carried out. A case of retained testis in the groin, or a case of ectopia testis, should be operated upon before the age of 8, in order to prevent atrophy and ensure spermatogenesis towards puberty.

A boy with one testis retained in the abdominal cavity should be operated upon before puberty for fear of malignant disease.

In the case of retention of both testes in the abdominal cavity, careful observation should be made as to whether there is a tendency to descend through patent inguinal canals at or about puberty. An absence of such patent canals, or any obscure abdominal trouble which may possibly be attributed to the retained testes, should indicate that the operation should not be further delayed.

Spencer Wells, in 1879, when recommending the use of pressure forceps, said he had operated on a man and removed a large testis which had been retained in the abdominal cavity.

Stiles, in 1906, and others since, have removed an abdominal testis, the pedicle of which had undergone torsion.

In 1907 Boesa removed an abdominal testis which had become sarcomatous before undergoing torsion of the pedicle.

In a man of 38, whose left testis had always been absent from the scrotum and who had had colicky pains for seven months, an abdominal tumour was felt resembling a kidney. This was found to be a sarcomatous testis weighing 1·1 kilos; the tumour was of the alveolar round-celled type of sarcoma which was undergoing necrosis. The patient recovered from the operation, but from what is known of the disease it is fairly certain that he was not cured. Indeed there is an entire absence of records of cure after a retained testis has once become malignant.

It has been found possible by Coley and others to bring down into the scrotum a testis retained in the abdominal cavity, and that on both sides. It will generally be best to operate on one side at a time. In the case of unilateral retention, with a well-developed testis in the scrotum on the opposite side, excision of the testis retained in the abdomen will be the procedure to be generally adopted. In the exceptional case of both retained testes being removed, recourse may be had to a homoplastic transplantation of a testis from a young man or boy accidentally killed.

Lydston of Chicago, in 1918, reported the following experience regarding implantation of a testicle.

Case I. A man aged 30 had both testes destroyed by septic infection following injury. He became quite impotent and signs of eunuchism began to show themselves. A boy aged 14 had been killed by being crushed, and six hours after his death his testes were removed and placed on ice for 33 hours. The testes were then implanted into the scrotum of the man. He had healed in two weeks; subsequently he lost 40 lb. of fat and eunuchoid signs disappeared. The implanted testes persisted, feeling rather smaller and harder than normal in a boy of 14. The man had also at the end of each persisting vas deferens an enlargement on one side the size of a grain of wheat, on the other that of a good-sized pea. He had recovered potency.

Case II. A boy aged 13 had suffered from double orchitis after vaccination (there is no mention of mumps). The orchitis was followed by atrophy. At 19 he presented the signs of a eunuch and an absence of those of virility. From a boy aged 15, who had been killed by carbon monoxide poisoning, the testes were removed 24 hours after death and kept on ice for 32 hours. They were then implanted into the prospective eunuch and healed well. 16 months later the implanted testes were the size of those of a boy between 12 and 14 years. Virility had become established, also the atrophied right testis had increased.

Kreuter, in 1919, reported the results of implantation obtained by Steinach and Lichtenstern. They transplanted the testis retained in the groin from one man into the scrotum of a man who had lost both testes from injury, and, after observing the result for two years, reported that the man had married and exercised sexual functions. In another case they implanted a testis likewise retained in the groin of a man into the scrotum of another who had undergone double castration for tuberculosis. After observing the result for a year, they found that sexual desire had revived and the man had married. Kreuter had had himself a third case in which the result was similar. His conclusion was that, whilst the graft underwent much atrophy, there persisted sufficient cells to maintain an internal secretion. Instead of this conclusion, a view may be held similar to that about thyroid grafting, mentioned in a previous number of *Medical Science*. viz. that the implantation stimulates to development fragments of the original testis and epididymis persisting at the end of the vas deferens.

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W. G. S.

INFECTION AND DISINFECTION OF THE HANDS

The subject of the disinfection of the hands has been actively debated since the introduction of antiseptic surgery. An important change ensued upon the introduction into general use of rubber gloves, although this has been found to be attended by some drawbacks. An infection of a finger is an everyday occurrence which may vary in importance from a trifle to a severe illness followed by permanent damage to the hand, or entail amputation in order to avoid death. Cases of death from such infections are continuously reported. Infections of the hand have come to be recognized as associated with certain occupations. The enormous number of communications which have been made upon the disinfection of the hands exhibit so much repetition that one can but conclude that a stage has been reached beyond which it is difficult for any new observations to be made. The infecting micro-organisms are found on the surface of the hands, in the superficial layers of the epidermis, and in the deep layers around the orifices of the ducts of the sebaceous and sweat glands. In these positions the organisms are doing no harm; only when carried through the epidermis into the dermis, whether by a puncture, by a cut, or by being rubbed in, do they begin to multiply and spread by the lymphatic spaces and channels.

The micro-organisms on the surface of the hands consist of staphylococci and streptococci of various degrees of virulence according to their source, and according as to whether greasy dirt has encouraged an increase in virulence. There are in addition gas-forming micro-organisms. Besides these, various specific varieties of germs may be present according to the objects with which the hands have come recently into contact. There is no doubt that most of the micro-organisms held upon the surface of the hands can be removed by thorough washing with soap in water. If the hands are kept clean as a matter of habit, it can be only rarely that any aid such as turpentine, benzine, ether, or alcohol is needed in removing fat and grease.

The question of germs existing in the outer layers of the epidermis after the hands have been rendered clean to the naked eye is the centre of the controversy. The soaking of the hands, already clean to the naked eye, in carbolic acid 1 in 40, sublimate or biniodide solution 1 in 2,000, in 70 per cent. alcohol, or some other solution, have been all advocated and opposed. The micro-organisms found in the superficial layers of the epidermis are *Staphylococcus albus* and streptococcus. Neither are in an active state, and can only become virulent after incubation in some suitable nidus. None of the innumerable bacteriological researches on the point are conclusive as to whether these germs in the outer layers of the epidermis of the well-washed hands of the surgeon do, as a matter of fact, infect an operation wound. The only evidence which can be brought forward is that the adoption of gloves has improved the results of surgeons who had cared for the state of their hands before. The above-mentioned solutions are widely believed to be of little use, because they cannot reach the germs in the epidermis without at the same time injuring the epidermal cells. Endless statements down to the present time have been made with regard to the use of 70–80 per cent. alcohol. The conclusion reached is that alcohol, whatever its strength, is not an antiseptic in the sense that it kills germs. But the soaking of the well-cleaned hands in 70–80 per cent. alcohol has been found by a number of surgeons to be a means of avoiding infection at surgical operations when rubber gloves are not worn. This effect is not produced by 60 per cent. alcohol or by absolute alcohol. The Germans during the war experienced a lack of rubber gloves, as also of soap. Gocht in 1916, confirmed by Stahlschmidt in 1917 and by Neufeld in 1918, and by Vogt in the Russian Campaign, used instead of soap finely-powdered plaster of Paris; after the hands had been well washed with this material they were soaked and rubbed with 70 per cent. alcohol. Hands so prepared were enabled to carry out all sorts of operations without setting up infection. One can only conjecture that the alcohol along with the plaster of Paris shuts off the micro-organisms in the epidermis from escaping during the conduct of a surgical operation. Micro-organisms in the deeper layers of the epidermis are lodged chiefly in and around the ducts of the glands and are carried outwards as the hand sweats; presumably, therefore, the alcohol tends to check this escape.

Seedorf has carried out an elaborate research in the problem of iodine disinfection from the point of view of both the bacteriologist and the surgeon. The experiments *in vitro* showed that iodine is most disinfectant in a 1 per cent. aqueous solution of potassium iodide and in alcoholic solutions (50 per cent.). Numerous experiments were carried out on sections of rats' tails which were highly infected and could easily be divided into fairly equal portions. They were treated with various disinfectants and in many different ways; it was found that a single painting with a 10 per cent. tincture of iodine reduced the number of bacteria considerably, but only after 3 or 4 paintings could more or less adequate sterilization be effected. When the strength of the tincture of iodine was reduced to 1 per cent., more frequent paintings were required to achieve the same results. Disinfection with alcohol alone was less effective than with alcohol plus iodine. It was also observed that previous washing with soap and water did not impair the disinfectant action of iodine even when it was applied to skin that was still moist. Indeed, this mechanical cleansing with soap and water contributed not a little to the subsequent sterility of the skin.

To test the actual efficacy of iodine in the disinfection of the human skin, Seedorf obtained small pieces of skin taken from the site of operation in three different surgical departments where the ritual of disinfection varied according to the views of different surgeons and the emergency of each operation. In all three departments a 5 per cent. solution of iodine in 90 per cent. of ethyl alcohol was used. In departments 1 and 2 emergency cases were shaved, washed with a 70 per cent. solution of ethyl alcohol, and painted twice, with a short interval, with tincture of iodine. The operation was performed about 5 minutes later. In department 3 emergency cases were thoroughly cleansed with soap and water, and at least 5 minutes elapsed between the first and second painting with iodine.

In cases which were not emergencies the skin was prepared in two stages with an interval of a day. In department 1 washing with soap and water was followed by the application of a 70 per cent. solution of ethyl alcohol and another of corrosive sublimate. A sterile dressing was then applied, and 6 hours later the skin was again washed with soap and water, alcohol and corrosive sublimate. The sterile dressing which was then applied was not removed till the patient was on the operating table, where another cleansing with alcohol was followed by the application of tincture of iodine. In department 2 the ritual of cleansing 12 hours before operation included both soap and water washing and one painting with iodine. This was followed in a few minutes by washing with 70 per cent. ethyl alcohol to prevent iodine dermatitis. A sterile dressing was applied over-night and was removed on the operating table where, a good 5 minutes before operation, a second painting with iodine was given. In department 3, soap and water, and 70 per cent. ethyl alcohol were employed 18 hours before operation, but no iodine was applied till 1 hour before operation. On the operating table the skin was cleansed with a 70 per cent. alcohol and a second painting with iodine about 5 minutes before the operation.

It was found that even when the skin had been subjected to thorough mechanical and chemical cleansing, it was still often infected. But the number of surviving micro-organisms showed a conspicuous fall as the result of successive iodine paintings carried out at regular intervals. Double iodine painting alone, when carried out with care, reduced the infectivity of the skin to a minimum. On the other hand, combined disinfection with soap and water, alcohol and sublimate did not satisfactorily reduce the number of micro-organisms even when it was carried out twice. As in the case of the rats' tail experiments, it was found that double iodine painting is as effective on moist, soap-washed human skin as on dry.

Another series of investigations showed that the depth to which iodine penetrates the skin varies with the amount applied. But even after repeated applications iodine does not reach beyond the stratum corneum, and it does not, therefore, penetrate to the deeper structures, such as the sebaceous glands. The choice of solvent, whether it was ethyl alcohol, propyl alcohol or a solution of potassium iodide, did not affect the depth to which iodine penetrated. But a comparatively deep penetration could be effected by increasing the concentration of iodine. This series of investigations also suggested that double iodine painting with an interval of 5 minutes, is peculiarly effective in disinfecting the skin. Seedorf is, however, doubtful as to the feasibility of rendering it perfectly sterile without simultaneously reducing its vitality.

Comparing his bacteriological examinations of the human skin with the post-operative histories of the patients from whom it was removed, Seedorf first excludes 36 per cent. of these patients because of an original cutaneous infection, post-operative drainage or death. Of the remainder, 90 per cent. showed healing by first intention, although the skin had proved to be sterile only in 42 per cent. Of the 10 per cent. that did not heal by first intention, 3 per cent. were cases of wound abscess, and 70 per cent. were cases of stitch abscess. In all these 10 per cent. the bacteriological examination gave positive results. These figures suggest that most of the bacteria which survive disinfection of the skin are comparatively harmless. In his advocacy of double iodine disinfection, Seedorf does not disparage preliminary mechanical cleansing with soap and water which he considers of importance especially in connexion with spore-forming micro-organisms.

The rules laid down in text-books for the cleaning of the hands of surgeons and nurses are apt to err by excess, especially when applied to all alike, from hands covered by very thin and dry skin to those in which the skin is thick and greasy. In the former case antiseptic solutions are likely to set up irritation and eczema which favours the penetration of germs. Nurses' hands are liable to become chapped when cleaning mackintosh sheets with carbolic acid. The repeated soaking in hot water and the use of rubber gloves also tends to soften the epidermis and render it more penetrable. A nail-brush may be a danger to delicate hands and the penetration of a bristle between the cuticle and the nail has been a frequent cause of infection.

Whilst surgeons and nurses must take the greatest care of their hands and nails, manicuring may be overdone, especially in the ridiculous attempt to make long and tapering nails. Körbl in Vienna has reported thirty-two cases of infection due to manicuring with infected instruments. In particular the pushing back of the skin from off the root of the nail exposes the sulcus of the ungual matrix to infection; tags of epidermis are snipped off so that absorptive areas of the epidermis are exposed. Self-manicuring may thus produce infection; but there are greater dangers from the apparatus of the professional manicurist, the same tools being used without being sterilized. Körbl found also that the leather strops and wipers, as well as the polishing paste were all infected. Streptococci, staphylococci, and anaerobe coliform bacilli were found: an infection in 4 cases of the same family, and 3 cases of erysipelas under the hands of the same manicurist confirmed the observations. The infection in many of the 32 cases was serious; 2 cases of paronychia were treated conservatively and healed in 5 days; 4 were cases of parungual panaritium, the pustule was opened and healing occurred in 7 days; 2 were cases of subungual panaritium, the nail was divided and healed in 3 weeks; 7 were cases of tendinous panaritium requiring several incisions, followed in 4 by sloughing of tendons and healing on the average in 5 weeks; in 5 the infection extended to the bone of the phalanx, after many incisions, in 3 there was a removal of the necrosed phalanx, and in 1 a general septicaemia, with healing on an average in 8 weeks; in 4 cases joints became involved with necrosis, destruction of the joints and sloughing of tendons, in 1 case amputation of a finger, and healing on an average in 10 weeks; in 2 cases the infective tenosynovitis extended to the palm with extensive sloughing of tendons, ending in stiff fingers and healing in about 3 months; in 1 case the infection extended to the arm which after many incisions healed in 3 months; in 1 case after an extension to the arm, amputation through the forearm became necessary; 1 case ran the course of a slight erysipelas and ended in a week: in 3 the course of erysipelas was more severe and ended in 3 weeks.

In considering infection of the hands in connexion with various occupations, abrasions of the epidermis and cuts which expose the dermis are more likely to receive immediate attention. The practice of applying an alcoholic solution of iodine has become widespread and is undoubtedly of good service; this casual use seems to be followed by fewer infections than attended the similar use of carbolic acid solution. But the application of iodine in the case of punctures is ineffectual, as also when virulent germs are rubbed in through intact epidermis. It is in such cases that there is apt to be delay, and meanwhile the organisms are incubating until they become virulent, when their spread cannot be controlled. Not only is the application of iodine a failure, but there is prevalent an erroneous practice, viz., the making of a small incision into the inflamed spot when at length the patient applies. The harm of such an incision is that the germs are pushed further into the absorbing tissue below the epidermis, whilst the margin of the cut epidermis gets stuck together so that the pus is for the time being retained.

It is a very common experience for a nurse to present a tender spot on a finger a few hours or less than a day after she has pricked the finger with a bluntish-ended pin. If the overlying epidermis is shaved off there is seen a dusky spot in the superficial layer of the dermis: it is coloured by blood extravasation and by necrosis set up by the organism carried in with the puncture. It is just as likely that the germs so carried in were on the finger beforehand, rather than on the point of the pin. The area of necrosis thus exposed may be treated with carbolic acid or iodine and then fomented; the infection is arrested and healing follows. There need be, however, no puncture, the organisms are rubbed in, whether from the surface, or because first a vesicle is formed in the deeper layers of the epidermis in which the organisms already in the epidermis multiply. An incision is quite wrong; what is required is the removal of the epidermis completely from over the vesicle which has now become a pustule.

The complication which may attend the use of rubber gloves is that organisms may enter through a puncture or rent and then become rubbed in. Hence dangerous infections of the hands of surgeons have arisen. Rents and punctures in rubber gloves are very liable to occur when carrying out bone and obstetric operations. A puncture through a rubber glove should be dealt with by shaving off the epidermis so as to expose the deepest end of the puncture; wiping with iodine is insufficient. Rubber gloves tend to rub in organisms, especially into the hair follicles on the dorsum of the proximal phalanges; then erysipelatous infection may develop rather than a whitlow. Some dispense with gloves when they are likely to be punctured or torn. Repeated applications of iodine may perhaps check the development of a superficial streptococcal infection when combined with an injection of antistreptococcal serum. Bier's method, a length of rubber tubing tied round the wrist, or a rubber glove rather tight at the wrist and cut away over the site of infection is a valuable method of checking acutely spreading erysipelas and lymphangitis. But this procedure has often failed because the site of infection has not been simultaneously laid open.

Heidenhain is most emphatic upon the hand being kept at rest. Whenever he or his assistants had cut themselves, the hand was kept at rest for the following 24–48 hours wrapped up in hot fomentations. Not only was work given up but the hand was not used at meals, nor in dressing or undressing. This precaution had been found to hold good through his 31 years of experience in surgery, and he quoted two instances of its neglect. An assistant pricked his finger at a post-mortem on a case of purulent peritonitis, and Heidenhain ordered him to keep the hand absolutely at rest in a sling. On returning from a holiday he learnt of the assistant's death. The arm had been put in a sling as Heidenhain had directed, but tempted by a fine evening he had gone to bathe and swim. A rigor occurred that same evening, the next day incisions were made and he died two days later. Heidenhain himself, whilst operating for an empyema, received a slight scratch on the back of the left middle finger through his rubber glove, but which did not penetrate to the dermis. As it seemed trivial he went on operating, wearing rubber gloves. He then kept his hand at rest for a day, but having letters to write, he used a typewriter for an hour. At the end of an hour he felt pain in the scratched finger. The next morning he had acute pain and swelling of the finger followed by a rigor, and lymphatic streaks appeared up the back of the hand and forearm. Multiple superficial incisions became necessary; he was ill for four weeks, healing took six weeks, and it was three weeks more before he could make full use of his hand.

Mock furnished a number of American statistics showing the gravity of neglect of occupational injuries to the hand and the disability which follows. There had been, however, a great reduction after the adoption in some cases of special measures, such as the immediate application of iodine.

75 per cent. of the reported cases of disability after injury to the hands had been in men engaged in stockyard occupations. Other statistics show a great prevalence among men working on railroads.

Five Insurance Offices had reported as follows:

(*a*) 15 per cent. of cases of total disability were due to hand infections. 20 per cent. of disability following injury to the hand were due to infection.

(*b*) 7–9 per cent. of all cases of disability were due to hand infection.

(*c*) 5 per cent. of all cases of disability were due to hand infection.

(*d*) 15–20 per cent. of all cases of disability were due to hand infection, especially after minor injuries.

(*e*) 65 per cent. of all minor injuries to the hand which occasion disability were due to infection.

The minor injuries consisted in pricks by pins or splinters, 'nail wounds', scratches, small cuts, cracked hands, blisters, contusions, and abrasions which were as a rule not reported until the infection had become established.

In various trades there was a repetition of minor accidents from similar causes which might be prevented, e.g. in one trade, the scratching by edges of tins, exposed ends of wire or nails, or pins in packages. It had been calculated that the average loss of time following minor infections of the hand averaged ten days per case. Immediate reporting and the application of iodine would cause a loss of not more than half an hour.

Cohn reported that tenosynovitis occurred among dressmakers who used large scissors and heavy pressing-irons. A form of chronic infection of the tendon sheath followed in those suffering from suppurative tonsillitis, pyorrhoea alveolaris, infective sinusitis and urethritis or gastric ulcer. It led to disablement and fixation of the tendons, and it was necessary to remove the source of the infection.

Hohmann and also Nagy reported a peculiar persistent hard oedema of the back of the hand which was traceable to the infection of extravasated blood and lymph. This followed squeezing and crushing of the hand and fingers. Although the inflammation need not be acute nor attended by fever or pain, incisions to give exit to blood-stained fluid were required. If this was not done there followed ischaemic rigidity and fibrosis of the muscles of the hand or adhesions or sloughing of tendons.

Usland describes a disease of the fingers of seal-hunters, known by them as 'spackfinger' It is familiar to, and much dreaded by, Norwegian seal-hunters because of its chronic course and the incapacity it inflicts. It is, apparently, confined to seal-hunters; all the eight cases seen by Usland in Aalesund, whence expeditions are made twice a year to the Arctic regions in quest of the Greenland seal (*Phoca groenlandica*) and the crested seal (*Cystophora cristata*) belonged to this class. The disease is unknown among sailors engaged in whaling expeditions and dog-fish catching. It may develop at any time of the year, but is most common at midsummer when the seal is changing its coat, which is often scabby and suppurating. As the seal-hunters are fully alive to the dangers of this disease, associating its development with scratches inflicted by the blubber knife, they note them carefully, and it is therefore possible to ascertain the incubation period of the disease with considerable accuracy. Its length is strikingly uniform; in the eight cases referred to it was never less than fourteen or more than twenty-one days.

Usland is convinced that the disease is due to a specific infection, although he has obtained no cultures on agar and bouillon except in one case in which he grew staphylococci. These were, however, probably due to a mixed infection. Direct staining methods also proved negative. The appearance of the finger is so characteristic that the patient always diagnoses 'blubber finger' before seeking medical aid. Both skin and subcutaneous tissues are greyish-yellow with a light brown tinge. The surface of the tissues on section is glistening, and they are of a curiously tense, elastic consistence. The skin itself is not thickened, and the transition between it and the subcutaneous tissues is ill-defined, but there is however, considerable proliferation of the fatty and connective tissue elements. The tendons are not affected, but their sheaths are yellowish-brown, like the more superficial structures. Early in the disease the finger is of a dark, cyanosed colour, never red as in ordinary whitlow. A characteristic feature is the absence of any appreciable haemorrhage when the finger is incised; there are only a few spots of blood, and after some seconds even friction will not force out more blood. There is also no pus, only a little yellowish-white fluid which oozes out on section. The absence of free haemorrhage is evidently due to thickening of the walls of the blood-vessels; this was so considerable in some of Usland's cases that the lumen of the vessels was completely obliterated. Around these vessels he found a round-celled infiltration, represented chiefly by lymphocytes, with an occasional plasma and young connective tissue cell. Another distinctive feature is the anaesthesia of the skin and soft tissues. The joints, on the other hand, exhibit hyperaesthesia, and the slightest movement provokes violent pain.

The disease shows a peculiar affinity for the bones and joints, and only a day or two passes between the first symptoms and the spread of the infection to the nearest joint. This becomes swollen, and the finger is held extended. During the next two weeks the other joints of the finger become involved. The wrinkles of the skin become obliterated, and the back of the hand, including the wrist, becomes oedematous. But the disease does not extend above the wrist, nor are the glands of the axilla and elbow enlarged. There is no fever or general malaise, the tingling pain is not severe enough to disturb sleep, and only when the finger is flexed is severe pain provoked. The joints grate on movement, and the X-rays show considerable changes both in bones and joints. The outlines of the joints are irregular, the adjoining bony tissue is rarefied, and after the disease has lasted about two weeks, periosteal deposits of bone are demonstrable.

The duration of this condition may be five or six months if it is left untreated. Meantime the patient is unfit for work, and in severe cases the joints become ankylosed and the finger useless. It may be so much of a hindrance that amputation is advisable. After a microscopic study of the disease, Usland adopted an elaborate scheme of treatment which included multiple incisions carried down to the capsule of the joint, passive congestion maintained during the night, and five to six hours a day of alternate sunlight and heat treatment. The improvement of the circulation achieved by these means was so great that in a few days the hyperaesthesia of the joints was sufficiently relieved to permit of active and passive movements. The profuse discharge from the longitudinal incisions never became purulent, but they were apt to close prematurely. As the condition improved and the anaesthesia diminished, the re-opening of these incisions became so painful as to necessitate general anaesthesia. In one case Usland succeeded in cutting short the disease after it had lasted ten to eleven days by excising the diseased tissues down to the bone.

The **hands of milkers** are liable to infection from the cow's teats, and conversely they transfer infection to the teats and udder, and to the milk.

The hands of milkers, like other farm labourers, have been naturally thickened and hardened by exposure and by work on the farm. This is a protection to the man so long as they are kept dry. But when the epidermis is softened and rendered sodden by washing in water and by contact with milk, the hands become more liable on exposure to become chapped, thus infection can more readily penetrate, and the chaps contain infecting organisms. To prevent the formation of chaps the milker smears his hands with milk; smearing with some form of petroleum tends to produce a sticky surface to which germs adhere.

The cow's faeces are necessarily semi-liquid, and even if ejected so as not to touch the buttocks, splashes may reach the udder. When the cow is driven, its semi-fluid motions run down and soil its perineum, buttocks, and udder. In the natural state air and sunlight soon dry the contaminating faeces, and presumably the calf is immune from harm. But cows under cover where neither air nor sunlight penetrate, and where the atmosphere is moistened by the breath of the cattle and their urine, faecal organisms are likely to remain virulent.

It is practically impossible to prevent soiling of the milker's hands, for they have in addition to groom the cows. In milking, if the teat is large and full, it can be held in the hollow of the hand and squeezed in a way which imitates the action of the calf's mouth and tongue. But in order to empty the udder of the last portion of the milk, or if there is any other difficulty, the thumb and finger are used to strip down the hollow teat. Hence germs may be rubbed into the milker's fingers, as well as into the teat.

Peiser of Breslau drew attention to a number of cases of whitlow which had occurred in milkers and were received in the course of milking and cleaning cows. The same thing had been noted to occur in Swiss dairies. The men presented infected wheals in the palm and on the flexor surfaces of the fingers. Between the wheals were deep fissures in which were found embedded fine whitish hairs from the cows' udders. The hairs were 2–3 mm. in length and were only observed on careful inspection. The fissures sometimes healed over, but broke out again until the hairs were removed.

Special infections by syphilis, tubercle, and anthrax of the fingers or hand have been often noted, and the characteristics of each are well-known. A case of whitlow infected by the diphtheria bacillus of Loeffler was described by J. D. Rolleston.

A boy, aged 3, with diphtheria of the fauces was treated by antitoxin from the 3rd day. The disease was complicated by disturbance of the cardiac rhythm, a nasal voice, and transient right hemiplegia and aphasia. On the 32nd day, the throat being then quite clear, bullae appeared on the fingers of the left hand, e.g. the side on which there had been no nervous disturbance. An ulceration followed the bullae but the ulcers exhibited no membrane. 3½ months after the commencement of the disease and 2½ months after the first formation of the whitlows the diphtheria bacillus of Loeffler was obtained from the surface of the ulcers. 8,000 units of antitoxin were thereupon administered and the ulcers which had persisted for 2½ months then healed in a week. Several other similar cases have been recorded.

Mauclaire described the infection by the bacillus of 'rouget du porc': altogether 66 cases had been recorded among pig-keepers as well as among laboratory workers and veterinary surgeons engaged in vaccinating animals against the disease. The course of the infection is much akin to erysipelas, and treatment by the serum is efficacious, but deaths have occurred, 3 among 7 cases under one observer.

Mauclaire's case was that of a farmer's wife, aged 50, who was cutting up a pig known to be infected but which was intended for food. In doing this she pricked the dorsal aspect of the 2nd phalanx of the right index finger with a point of bone and caused a little bleeding. Two days later she was suffering from an erysipelatous infection attended by high fever, malaise, headache, and vomiting. The point of infection showed a scarlet-red patch similar in colour to the patches about the ears, belly, and inner aspects of the limbs which are the manifestations of the disease in the pig. Outside the scarlet-red patch was a dusky-red oedema which did not extend beyond the dorsum of the hand and had not the sharp outline of the spreading margin of erysipelas. There were some lymphatic streaks running up the arm to the slightly swollen axillary glands. There was some throbbing of the finger, but not severe pain, and there was no tendency to suppuration. The chief feature was the severe general toxinaemia which under treatment by the specific serum subsided within a week. There were no signs of the severe complications which occur in the pig, the enlargements of the liver, spleen, and lymphatic glands in general.

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W. G. S.
C. L.

MUSCULAR TONE AND THE SYMPATHETIC SYSTEM

Changes in the tone of the skeletal muscles are amongst the most prominent signs of organic nervous diseases. Thanks to Sherrington's analysis we know the biological significance of the tonic contraction as a postural reflex, and we know how it is modified by alterations in the state of the central nervous system; but there is still considerable doubt as to the exact nature of the tonic contraction in the muscles themselves. There is an obvious difference between the forcible and easily fatigued contraction which results from a voluntary effort or a phasic reflex and the less powerful but more sustained tonic contraction which occurs in the postural reflexes. In some invertebrates there is little doubt that the two kinds of contraction are due to two different varieties of muscle-fibre, and it is often held that in the mammaliam muscle these two contractile mechanisms have become fused into a single fibre. The simplest expression of this view is to be found in Bottazzi's theory which holds that a muscle-fibre is made up of two distinct contractile elements, the fibrils and the sarcoplasm, and that these can contract independently, the former giving rise to the powerful phasic contraction, and the latter to the continued tonus. The evidence is conflicting; in favour of the dual theory is the fact that the tonic contraction needs a very much smaller expenditure of energy than the phasic contraction, but against it is the fact established by Buytendyk, and confirmed by Einthoven and by P. Hoffmann, that a muscle in tone shows a rapidly oscillating electric response of exactly the same type as that found in a voluntary contraction.

During the last ten years, however, an effort has been made to show that the tonic contraction has at least an entirely different innervation from that of the phasic contraction. This suggestion arose from the discovery by Boeke of non-medullated nerve-fibres supplying skeletal muscle. Boeke found these fibres in every muscle he investigated, and, by studying the degenerations due to section of different nerve-roots, he was able to show that the fibres were derived from the sympathetic system. This work has met with general acceptance, and it must be taken as an undoubted fact that voluntary muscle has a double nerve-supply composed of medullated fibres from the anterior horn of the cord and of non-medullated fibres from the sympathetic ganglia. The tonic function of these sympathetic fibres is much more doubtful. It has been upheld by de Boer, and he has brought forward a series of experiments to show, that after destruction of the sympathetic chain on one side in the frog the muscles on that side exhibit a distinct loss of the tonic element in contraction. He states that the muscles on the affected side hang more limply when the frog is suspended by the jaw, that on the cessation of the circulation they do not develop *rigor mortis* as rapidly on the operated as on the intact side, and that the muscles on the operated side relax more rapidly after a reflex or directly excited twitch. These results have been examined by Yas Kuno, Lopez and Brücke, and by Dusser de Barenne. Kuno repeated many of de Boer's experiments on frogs, and concluded that the differences he described were due entirely to the effects of vaso-dilatation in the limbs deprived of their sympathetic supply. Lopez and Brück worked on cats and reached the same conclusion. Dusser de Barenne agreed with de Boer that destruction of the sympathetic on one side caused a small decrease in the tone of the muscles on that side, but he found that the loss of tone produced by cutting the posterior root was very much greater, and he could detect no difference in the rate of development of *rigor* on the two sides when circulatory changes were excluded.

Direct stimulation of the sympathetic or injection of adrenalin has no effect on muscular tone. This, however, is not a fundamental objection. Langelaan, accepting de Boer's theory, has argued that the sympathetic is concerned with 'plastic tonic', i.e. with the maintenance of the muscle at a particular length, and not with 'contractile tone'. His experimental evidence has little bearing on the nature of the nerve-fibres which are responsible for plastic tone, but if the conception be accepted it is clear that the stimulation of these fibres could not be expected to cause a change in length, since their function is to preserve the existing length of the muscle unchanged.

On the other hand, there is an important body of evidence which is directly opposed to the view that the sympathetic system has anything to do with either the development or the maintenance of tone. It is generally agreed that the condition known as decerebrate rigidity is due to a great increase in the tone of those muscles which are most concerned in maintaining the posture of the animal against the force of gravity. Indeed, the tonic contraction is so well-marked in decerebrate rigidity that we owe most of our knowledge of the phenomena of tone to the study of the decerebrate preparation. If the tonic contraction is dependent on sympathetic innervation we should expect to find that the production of decerebrate rigidity would be profoundly affected by destruction of the sympathetic ganglia. Experiments to test this point have been carried out by Dusser de Barenne, van Rijnberk, and Cobb. All the investigations were performed on cats; the abdominal sympathetic chain on one side was destroyed either before or after decerebration, and the tone of the muscles on the two sides was compared by observing the attitude of the limbs, the resistance to passive movement, &c. Dusser de Barenne found a diminution in tone on the operated side in five cases out of nine: in the remaining four he could detect no difference; van Rijnberk found no constant difference in a series of nineteen experiments, and Cobb found none in a series of six. It appears, then,that although removal of the abdominal sympathetic chain is occasionally followed by a diminution in the tone on that side, yet in the majority of these experiments the loss of the sympathetic supply makes no difference; the rigidity is developed and maintained as well on the operated as on the intact side. Van Rijnberk has performed the converse experiment of cutting the ventral roots supplying the hind limb and leaving the sympathetic supply intact. In this case no rigidity is developed after decerebration.

Thus, all the recognized phenomena of tone can be produced in muscles which have been deprived of their sympathetic supply, whereas none of them can be produced when the ventral roots are cut. It is difficult to avoid the conclusion that the tonic contraction is set up and maintained by impulses passing down the motor nerves from the ventral horn of the cord. There is no doubt that the skeletal muscles are connected to the sympathetic system, but the sympathetic fibres are not concerned with tone. What their function may be is a question which must be left for future research; at present we have only one reason for supposing that they have any function at all, and that is the fact that they exist.

Thus the attempt to prove a dual innervation for the tonic contraction and the twitch has failed, and it is still uncertain whether we have to deal with a dual contractile mechanism in the skeletal muscle-fibre or whether a single mechanism will not suffice.

For further details the reader is referred to the pages of the *Archives Néerlandaise de Physiologie* and to the recent review by Prof. Ducceschi.

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E. D. A.

ABSTRACTS

SURGERY

Longo, L. Su un interessante caso di lipoma sottomucoso ostruente del cieco. [**Submucous lipoma of caecum.**] *Policlin.* (Sez. Chir.), 1920, **27**, 105.

The patient, a woman aged 47, had always suffered from constipation. Acute symptoms had been present for six weeks, consisting of attacks of abdominal pain, colicky in character, and more marked in the right flank; these occurred shortly after meals and lasted from three to four hours. Later, the attacks, increasing in severity, became associated with vomiting and obstinate constipation. On examination, the abdomen was somewhat distended and there was some feeling of resistance on palpating the right iliac fossa. Laparotomy was performed and a submucous lipoma, of the size of an orange, found projecting into and partly obstructing the caecum. The tumour was excised, with a small portion of the wall of the bowel at the site of attachment. The mucous membrane covering the tumour was slightly eroded.

From a study of the literature, Longo finds that lipoma occurs with about equal frequency in the large and small intestines. It is usually solitary, although cases of multiple lipomata in the region of the caecum are on record. Though usually small, these tumours have been known to reach the size of an adult head. Their point of origin is almost always in the submucous layer of the bowel; exceptionally their position is serous or subserous, and in this case they are generally connected with the large intestine and probably arise from the appendices epiploicae. Subserous lipomata, inasmuch as they cause no protrusion into the lumen of the bowel, are without symptoms until they reach a considerable size and exercise pressure on surrounding organs. Submucous lipomata, on the other hand, are liable to give rise to partial obstruction through narrowing of the lumen of the bowel, or to intussusception. The former appears to be the rule when the tumour is situated in the large intestine, the latter when in the ileum.

T. W. P. L.

Angeletti, E. Sulla spalla vara. [**Humerus varus.**] *Chir. d. organi di movimento*, 1919, **3**, 513.

Angeletti describes six cases of humerus varus, the ages of the patients varying from 12 to 45 years. The symptoms associated with the condition were in every case first noticed in infancy or childhood, and consisted in defective growth in length of the arm, and limitation of the movement of abduction. At the time of observation the shortening of limb varied, in the several cases, between 3·5–8 cm. and abduction was limited to 25–45°. The right shoulder was involved in three cases, the left in two:

in one case, a cretin, the condition was bilateral. The histories throw little light on the aetiology: in one case a trauma preceded the onset of the symptoms; in another, pus had been evacuated from the upper part of the arm in early infancy. Evidence of the presence of congenital syphilis and rickets is absent in all the cases.

The deformity of the upper extremity of the humerus, well shown in a series of radiograms illustrating the article, is singularly uniform. The inwardly curving portion of the upper and inner part of the bone, which supports the lower margin of the hemispherical articular surface and produces its characteristic tilt, is undeveloped; so that the articular surface appears to be sessile on the upper end of the shaft and looks almost directly inwards. The upper end of the bone, viewed from the front, is, therefore, club-shaped, the great tuberosity forming its highest point. In addition, there is a more or less well-marked curvature of the upper part of the shaft with the convexity directed outwards. Angeletti states that in the radiograms from the two youngest patients (12 and 16 years) it was possible to demonstrate that the inner half of the epiphyseal line was consolidated, the outer half being still cartilaginous, and he attributes the deformities and the defective growth of the bone to this condition.

Mention is also made of humerus varus occurring in connexion with rickets and achondroplasia. T. W. P. L.

Taddei, D. Il quadrilatero gessato per la cura delle fratture diafisarie e cervicali dell' omero e per l'immobilizzazione della spalla. [**Quadrilateral splint for fractures of the humerus.**] *Chir. d. organi di movimento*, 1919, **3**, 587.

Taddei writes: 'Clinical experience has proved that in the treatment of fractures of the shaft and neck of the humerus, as in all cases in which immobilization of the arm is likely to be followed by stiffness or ankylosis, the arm ought to be placed in horizontal abduction. The reason for this principle, now fully recognized, but little known among medical men in general, is obvious: in ankylosis in adduction the compensatory movements of the scapula cannot be brought into use.

'In fractures of the humerus I have for some time used weight extension applied to the forearm, the arm being abducted to the extent of 90°–130°. The method is good in special cases and gives good results; but it has the inconvenience, in ordinary cases, of keeping the patient in bed, which is not readily tolerated for any length of time. Weight extension and extension by elastic tubing are not, in my experience, well borne by the patient. In place of these methods I have used, often with the best results, the triangular splint designed by Middledorf-Port.' Finding, however, that this was at times liable to cause pain and oedema of the forearm, Taddei substituted a quadrilateral splint in place of the triangle with results that proved entirely satisfactory. The measurements for this splint are taken on the healthy side of the patient, with the arm horizontally abducted and the elbow flexed to about 110°, the four sides of the quadrilateral corresponding to the distances from the axilla to the bend of the elbow, from the bend of the elbow to the metacarpo-phalangeal line, from the latter to the iliac crest, and from this back to the axilla, thus completing the quadrilateral. For constructing the splint, four wooden pegs are fixed on a board in position corresponding to these measurements and so as to form a right angle at the point corresponding to the axilla. Several turns of plaster of

Paris bandage are then wound round outside the pegs and allowed to set. A thin strip of wood, inserted diagonally between the angle at the iliac crest and that at the elbow, serves to strengthen the splint and prevent it yielding under the weight of the arm. The quadrilateral is retained in position by three or four turns of a bandage passed from the iliac angle over the opposite shoulder, a second passed circularly round the body to include the vertical portion of the splint, and a third circularly round the forearm and lower part of the arm, fixing the upper and outer sides of the quadrilateral.

Besides immobilizing the arm in abduction, the apparatus has the further advantages (1) of exerting continuous traction, due to the weight of the forearm resting on an inclined plane, (2) of permitting massage to be employed from the outset, the shoulder and seat of fracture being completely exposed, and (3) of being well tolerated by the patient. T. W. P. L.

Putti, V. La ricostruzione dei legamenti crociati del ginocchio. [**Reconstruction of the crucial ligaments of the knee.**] *Chir. d. organi di movimento,* 1920, **4**, 96.

Putti records a successful operation for reconstruction of the crucial ligaments of the knee-joint, based on the method of Hey-Groves. The right knee was ankylosed in the extended position, consequent on a shrapnel wound. Arthroplasty was performed and a flap of fascia lata interposed between the ends of the bones. At this operation the crucial ligaments were found to be represented by a few strands of fibrous tissue, which tore through on flexing the joint. The results of this operation were on the whole satisfactory; but after a time a certain degree of lateral mobility in the joint became manifest, together with a sliding movement of the tibia on the femur in the sagittal plane, necessitating the use of a cylindrical knee-splint, jointed so as to admit of flexion and extension only. The splint becoming irksome to the patient, a further operation was undertaken. The tissue destined to replace the ligaments was taken from the left fascia lata. *Lateral ligaments.*—Two flaps of the fascia, 4 × 10 cm., folded in their length to form bands, were passed subcutaneously to the sides of the femoral and tibial condyles and fixed to the bones by means of metal screws. *Anterior crucial ligament.*—A flap of fascia, 4 × 20 cm., was rolled on itself to form a cord, the shape being retained by a stout silk thread passed longitudinally through it. Through a small cutaneous incision a canal, 10 mm. in diameter, was drilled through the bone, starting superiorly on the outer surface of the lower end of the femur and passing obliquely downwards and inwards through the femoral condyle and upper extremity of the tibia, opening on the antero-internal surface of the latter about four finger-breadths below the articular surface. The canal measured 16 cm. in length. To control the passage of the perforator across the articular cavity the latter was brought into view by means of a short parapatellar incision. Into the canal thus prepared a flexible metallic rod furnished with small terminal pincers was introduced and by its means the fascial cord drawn through the canal. The extremities of the cord were then fixed to the bones by metallic screws, and the knee placed in plaster of Paris in a position of slight flexion. Mobilization of the joint was commenced on the 20th day. Examined five months later there was complete power of extension, active flexion to 60°, freely movable patella, and no sign of lateral or sagittal mobility. The patient could walk rapidly without the need of any supporting apparatus. Alwyn Smith has recorded (*Brit. J. Surg.*, **6**) three cases in which he modified the operation of Hey-Groves by utilizing a single strip of fascia to perform the functions both of the anterior crucial and of the internal lateral ligaments. Putti has modified this method slightly by using two bands instead of one, having found that there was some risk of the single band necrosing at the point where it turns round the margin of the lower orifice of the canal. T. W. P. L.

Vernoni, G. Sopra un caso di paralisi del radiale da neurite apoplettiforme, con emorragie cutanee nel territorio dello stesso nervo, e presenza in circolo di un B. pseudodifterico patogeno (emorragico). [**Recurrent paralysis of musculo-spiral nerve.**] *Chir. d. organi di movimento*, 1920, **4**, 29.

Putti, V. Sovra un caso di paralisi recidivante bilaterale del radiale. [**Recurrent paralysis of musculo-spiral nerve.**] *Chir. d. organi di movimento*, 1920, **4**, 45.

When the patient, a girl of 13, came under observation, the following conditions were present: On the outer surface of the right arm, at the junction of the lower and middle thirds, there was an ecchymosis of the size of a crown-piece, and there was well-marked wrist-drop, with an anaesthetic area over the dorsum of the first metacarpal bone and interosseous space.

Putti cut down on the musculo-spiral nerve in the lower third of the arm and found it free from adhesions to the surrounding parts, but somewhat opaque in about half an inch of its length. Below this spot the nerve was diminished in thickness and gave no reaction on electrical stimulation. On incising the sheath of the nerve a small blood-clot, apparently of old standing, was found between the sheath and the nerve trunk. This was readily removed, the nerve beneath being grey and indurated. The nerve was then enclosed in a piece of calf's artery and the sheath sutured with catgut. On examination eight months later the paralysis and ecchymosis had disappeared. Subsequently attacks of temporary paralysis occurred at intervals in both arms, accompanied in every case with ecchymosis in the skin of the corresponding limb. Thus in the six years during which the patient was under observation the right musculo-spiral nerve became paralysed four times, the left three times. Details of the previous history of the case are given in Vernoni's paper. In addition to the petechial eruptions, urticarial and papular rashes had appeared from time to time, the former limited to the hands and feet, the latter having a more general distribution. Petechiae appeared nowhere but in the paralysed limbs. Vernoni was able to isolate a pseudo-diphtheritic bacillus by haemoculture.

T. W. P. L.

Fieschi, D. Nefropexia con rete di gomma. [**Nephropexy by means of an elastic net.**] *Arch. ital. di chir.*, 1920, **1**, 671.

The advantages claimed for Fieschi's operation for the fixation of movable kidney are: The avoidance of healing by second intention, which is inevitable in methods in which gauze is left in contact with the kidney in order to provoke adhesions; the avoidance of all possibility of recurrence; and the rapidity of the cure, the patient being able to resume work within a fortnight without any danger.

The kidney is placed in a net, which is shaped to it and fits somewhat loosely, and by this means is strung up to the eleventh rib. There is no possibility of further prolapse and the external wound can be closed immediately. Objections have been made to the method on the ground that during the operation the net is difficult to construct. This objection has, however, been largely overcome by recent improvements, and more especially by having the net partly constructed beforehand. Normal kidneys of different sizes are hardened in formalin and kept as models, the size to be chosen in any particular case being determined as far as possible by palpation of the movable kidney. On the model chosen a net of elastic strands is constructed, consisting of two vertical loops (the elastic 4 mm. in thickness), which pass round the lower pole of the kidney and serve to support it, the upper ends being attached to the rib; and five horizontal strands (2 mm. in thickness) passing horizontally round the kidney. At the points of crossing the strands are united by means of fine silver wire. In the net thus prepared, the upper three horizontal strands are, in the first instance, left unknotted towards the hilum, in order to allow of the introduction of the kidney. At the operation the insertion of the kidney and the fixation of the three strands is a matter of a few minutes only. The upper ends of the vertical strands are then passed round the eleventh rib, after the pleura has been detached for about 2 cm., and secured with silver wire.

During the last four years Fieschi has performed this operation with success in six cases. T. W. P. L.

Scheuermann, H. Kyfosis dorsalis juvenilis. [**The aetiology of dorsal kyphosis in adolescence.**] *Ugesk. f. Læger*, 1920, **82**, 385–93.

Scheuermann has come to the conclusion that dorsal juvenile kyphosis is not due, as generally supposed, to defectiveness of the muscles of the back, but to injury to the vertebral column in the lines of growth between the bodies of the vertebrae and their epiphyseal rings. The disease is therefore, in his opinion, analogous to that of Calvé-Perthes or osteochondritis deformans juvenilis coxae, and it should be termed osteochondritis deformans juvenilis dorsi.

The material investigated consisted of 105 cases of dorsal kyphosis observed at a home for cripples. In 60 of these cases there was no lateral curvature, and in the remaining 45 the dorsal kyphosis was combined with slight lateral curvature. Although girls suffer more than boys from spinal curvature taken as a whole, in this particular class of curvature the proportion of males was as great as 88 per cent. The age at which it was most common was from 15 to 17. Strenuous work played an important part, for the condition was most common in lads employed on the land. Scheuermann devotes much attention to the X-ray picture, and he stresses as characteristic of this disease the wedge-shaped condition of the bodies of the vertebrae seen from the side. A study of spinal deformities in the horse has led him to find the dorso-lumbar lordosis of the horse to be analogous to the juvenile kyphosis in man.

With regard to treatment and prognosis he is agnostic and pessimistic. He has frequently attempted to keep the spine fixed for a considerable period in a position of lordosis by bandaging, but without noteworthy effect. Once the kyphosis has become established (and the patient does not seek surgical aid at an earlier stage) normal conditions cannot be restored. If the patient complains of pain in the back and of feeling overworked, he should be kept in bed for a week or two. Further development of the kyphosis may then be combated by a plaster-of-Paris support, fitted in a position of suspension or lordosis, and worn for some months. Gymnastic exercises and massage of the muscles of the back may then be given a trial. But Sheuermann seems to consider such interference rather as a placebo than as calculated to effect permanent, objective improvement.

C. L.

Borelius, J. Zur operativen Behandlung gewisser Ascitesformen, besonders Ascites bei Morbus Banti. [**The operative treatment of ascites with special reference to that of Banti's disease.**] *Acta. Chir. Scandin.*, 1920, **52**, 373–81.

Professor Borelius gives an account of a case of Banti's disease of aetiological and therapeutic interest. The patient was a married woman, born in 1878. In 1909 she noticed a swelling of the abdomen, and in 1912 she was admitted to hospital with well-defined Banti's disease. Paracentesis was frequently repeated, and arsenic and various other drugs were given with indifferent results. In 1913 Talma's anastomosis operation was performed, in the course of which the spleen was found to be enlarged and plastered by extensive adhesions. The liver was cirrhotic, and its surface uneven. A few weeks after this operation the rate at which fluid formed in the abdominal cavity began to slow down, and during 1914 and 1915 paracentesis was performed only once every sixth month. But by January 1916 the ascites had again become so troublesome that another operation was necessary. This time the abdomen was opened in the flank, free fluid was withdrawn, and a piece of fascia, taken from the thigh, was made into a tube with catgut sutures. One end of this tube communicated freely with the peritoneal cavity, while the other opened into the muscles of the lumbar region. After this operation only four more paracenteses were necessary, and since June 1916 they had not been performed.

Discussing this case, Borelius finds it remarkable that a patient, who in 1912 had reached the ascitic stage of Banti's disease, should not only be alive 7 years later, but also perfectly fit for work and with so little ascites that for more than 3 years paracentesis had been unnecessary. There was no sign of syphilis; this was undoubtedly a typical case of Banti's disease. Although in other forms of cirrhosis of the liver ascites may disappear spontaneously, this has never been known to happen in true Banti's disease. The spleen is commonly regarded as the primary cause of Banti's disease, and its extirpation accordingly recommended. But if this hypothesis be true of every case, how could measures confined to relieving a single symptom, such as ascites, effect such lasting improvement as in this case?

C. L.

Michaëlsson, E. Resultaten av den operativa behandlingen for hypernefrom. [**Results of operations for hypernephroma.**] *Hygiea*, 1920, **82**, 220–32.

Michaëlsson's material consists of 30 cases of hypernephroma operated on in the period 1896–1915 at the Seraphimerlazarett. The post-operative observation period was thus 4 years or more. Only 7 of the patients were still alive. Four had died at the time of operation, 6 had died of recurrence of the disease within 3 years, and 3 had died from recurrence more than

3 years after the operation. Ten had died of diseases other than hypernephroma, and of these, 5 had died within 18 months of the operation. Referring to the microscopic examinations made in most cases, M. admits that it is difficult and almost impossible to gauge the malignity of the new growth by histological scrutiny. But in some cases it is possible to establish a correlation between the histological and clinical signs of malignancy. Discussing the literature of the subject, he finds that the malignancy of hypernephroma has commonly been underrated, partly because some writers have accepted a post-operative observation period of 3 years or less as adequate. In this connexion it may be noted that in one of M.'s cases the disease recurred 10 years after operation, and in another 4½ years after operation. C. L.

Sundberg, H. Fall av opererad embolus arteriae femoralis. [**Successful removal of an embolus from the femoral artery.**] *Hygiea*, 1920, **82**, 1–12.

Sundberg's patient was a farmer of 63 who had been in hospital for a few days on account of heart disease when his left leg suddenly became painful. The pain extended up the limb, from the instep to the thigh, and other signs of embolism, such as loss of pulse, numbness, and coldness of the limb left little doubt as to the diagnosis. But for various reasons it was not possible to operate till 12 hours after the onset of the pain. Under local anaesthesia, supplemented by an injection of morphin, the common femoral artery was exposed and clamped well above the upper limit of the clot. The artery having been incised and the clot having been found to end about 2 cm. above the bifurcation of the femoral artery, gentle traction was exerted on it and its removal in one piece was successfully accomplished. It measured 86 cm. and had therefore evidently extended to the sole of the foot. The artery was sutured with paraffin-soaked silk, care being taken not to include the intima in the sutures. Convalescence was delayed by thrombophlebitis of the left calf, but complete recovery was ultimately effected, and there had been no relapse 2 months after discharge from hospital. Sundberg's digest of the literature of this subject shows that of 20 cases in which operation for embolism was attempted (embolism of the pulmonary arteries being excluded) only 6 were permanently successful.

C. L.

Backer-Gröndahl, N. Narkosedödsfald. [**Deaths due to a general anaesthetic.**] *Supplement to Med. Rev.*, 1919, **36**, 1–70.

This 70-page study covers a period of 12 years and is based on necropsies performed at the Pathological-Anatomical Institute of the Rikshospital in Christiania. The material consists of 42 cases, in most of which the liver, kidneys, and lungs were examined, and in some of which the brain, spinal cord, suprarenals, thyroid, and solar plexus were included in the examination. Separate sections of the work are devoted to the post-mortem investigations of various organs and groups of organs.

In his *résumé* the author points out that in some cases death, or at any rate severe complications, can be traced to disturbances of the intracranial pressure. Chloroform at any rate, and ether in all probability, are capable of provoking severe oedema of the brain, the occurrence and significance of which have hitherto been almost wholly ignored. This oedema of the brain, resulting from narcosis, appears to be most common in children; but the author has found definite signs of it also in adults. The following case (No. 23) is illustrative.

A girl, aged 10 years, suffered from acute appendicitis. Under ether anaesthesia appendectomy was performed. She was very restless during the following night, and next morning she was delirious, pale, and cyanosed. The pulse was 168, the temperature 40–2° C. Death occurred about 24 hours after the operation. At the necropsy the heart and lungs were found to be practically normal, the thymus was rather small (12 grm.), the peritoneal cavity contained about 70 c.cm. of fibrino-purulent fluid, the mesenteric glands were enlarged, the kidneys showed slight degenerative changes, and the spleen was soft and somewhat enlarged. The brain was large (1,380 grm.). The pia mater was much injected, the gyri were very flat, the sulci shallow. On section, the brain substance proved to be very hyperaemic, but no pus could be found. The microscopic examination of the brain showed marked hyperaemia which extended also to its meninges. There were numerous small haemorrhages into the brain, but no sign of inflammation.

This oedema of the brain is probably toxic and is comparatively common in children because the regulation of the intracranial circulation is still imperfect. The most significant sign of cerebral, narcotic, or post-narcotic compression is cessation of respiration, and it is probable that respiratory failure during general anaesthesia, when it is not accompanied by a fall of blood-pressure or failing action of the heart, is to be traced to increased intracranial pressure due to transitory oedema of the brain and an increase of the cerebrospinal fluid. The author has found oedema and hyperaemia of the brain even when several days have elapsed before the effects of narcosis have culminated in death.

The author describes every variety of narcosis poisoning, ranging from rapidly fatal symptoms of general poisoning to slowly developing injury to single organs. With reference to these protracted cases he points out that a still less severe poisoning occurs in the majority of cases in which a general anaesthetic is given. Indeed, he makes out that the administration of a general anaesthetic always, or at any rate often, provokes degenerative changes which, though they may not be fatal, injure the patient, delaying his recovery for a considerable period. Though he finds that chloroform is more dangerous than ether, he notes that the latter, even when given by itself, sometimes induces fatal degenerating changes. As for the tendency to explain mortalities under general anaesthesia by assuming a morbid predisposition to degenerative changes, it is supported by imperfect evidence; both chloroform and ether are powerful poisons whose action differs rather in degree than in quality. C. L.

TANDBERG, O. En ny seneplastik ved platfot. [**A new plastic operation on tendons for flat-foot.**] *Supplement to Med. Rev.*, 1919, **36**, 117–20.

After reviewing the various operations for flat-foot, and noting that the frequency of relapses appears to be directly proportional to the intricacy of the operation, Tandberg describes an operation which he has devised, and found successful in the following case.

A boy, aged 7 years, had suffered progressive discomfort from flat-foot ever since he began to walk. He had not suffered from rickets or poliomyelitis. At the age of 6 a small wedge-shaped tarsectomy was combined with shortening of the tendons of the tibialis anticus and posticus muscles. The foot was put up in plaster, and a specially fitted boot was provided, but the arch of the foot soon collapsed, and when he was admitted to Tandberg's hospital the condition was worse than before the operation. He complained of pain in the left foot on walking, and limped noticeably. The skin about the old operation wound was thin and tender. The Achilles tendon was not appreciably shortened, and the range of active movement about the ankle was only slightly limited. There was also only slight atrophy of the calf muscles. When weight was thrown on the limb, the foot flattened out completely, and the head of the astragalus and the scaphoid bone became very prominent.

To repeat the original operation and remove still more of the bony arch by a wedge-shaped excision did not seem promising, so an attempt was made to restore the arch by tightening up the tendon of the tibialis anticus by a device not involving any tendon suture. Under ether anaesthesia the foot was manipulated into the desired position. Then a curved incision was made from the internal malleolus and carried forward over the most prominent part of the inner side of the foot. The tendon of the tibialis anticus was exposed and freed by division of the median portion of ligamentum cruciatum, close to its attachment to the scaphoid bone. After division of the tibio-navicular and navicular-cuneiform ligaments, a deep furrow was gouged in the bones of the instep with an osteotome and narrow resection forceps (dental resection forceps), beginning just behind the insertion of the tendon of the tibialis anticus. From this point the furrow was carried backwards in a curved line across the plantar surface of the first cuneiform bone and that of the scaphoid bone. The furrow was then continued upwards in a curve across the head of the astragalus towards the course of the tendon as it passes in front of the tibia. The tendon was now pulled out of its normal position by a blunt hook and fixed in the bony furrow, while the instep was arched as much as possible by forcible manipulation. The tendon was kept in its new bed by the promontory of bone formed by the median plantar corner of the scaphoid bone. The divided ligaments were now sutured and the wound in the skin closed. The arch of the instep was now so marked, and the position of the foot was so satisfactory, that the contemplated division of the Achilles tendon was found to be superfluous. The foot was secured in plaster in an over-corrected position. The wound healed without reaction. After about 7 weeks the patient was discharged with a plaster splint. This was removed a month later, when the arch of the foot was found to be maintained, and the range of movement satisfactory. The foot was now fitted with a support modelled from a plaster cast. On examination about 8 months after the operation the boy still limped, but less than before. He no longer complained of pain, and though the foot was still somewhat pronated, with abduction of the tarsus, the arch of the instep was well maintained on the inner side of the foot. Dorsal and plantar flexion were normal, but there was still some limitation of active supination. When weight was thrown on the limb, the inner side of the foot only just touched the ground, and most of the weight was distributed between the heel and the ball of the big toe.

Comparing his operation with Müller's, Tandberg points out that this surgeon detaches the tendon of the tibialis anticus completely from its insertion, and bores a channel through the scaphoid bone, pulling the tendon through this channel and suturing it to the plantar surface of the bone. The effect of the author's operation is the same; the scaphoid bone is given a powerful support, the supinator action of the tibialis anticus is augmented, and the pull of the tendon in its new position on the cuneiform bone and the base of the first metatarsal bone probably helps to correct over-abduction to a certain extent. The technique of this operation is simple, and it entails no tendon suture, for the strong natural attachment of the tibialis anticus to the cuneiform and first metatarsal bones is left intact. The after-treatment should follow conventional lines, with the wearing of specially fitted boots. If the Achilles tendon happens to be much contracted, its prolongation by tenotomy may be necessary. Tandberg's operation may be combined with a wedge-shaped excision of bone, provided enough of the bony arch is left to afford a promontory preventing the tendon of the tibialis anticus slipping back again into its normal position. Probably this operation is best suited for children with relaxed and plastic insteps.

C. L.

NEUROLOGY

Hurst, A. F. What the war has taught us about hysteria. *Contributions to Medical and Biological Research: dedicated to Sir William Osler*, 1919, i, 600.

In a most 'suggestive' general review Hurst summarizes conclusions derived from his experience at the Seale Hayne Neurological Hospital at Newton Abbot in Devon, and for the most part already published in greater detail elsewhere. Among the more interesting of his observations and conclusions is his definition of hysteria as 'a condition in which symptoms are present which have been produced by suggestion and are curable by psychotherapy': hysteria does not exist apart from hysterical symptoms and has neither mental nor physical stigmata. Hurst then advances the view that many of the physical signs commonly regarded as indicative of organic disease are actually hysterical in origin. Thus, he is convinced that Head's areas of cutaneous hyperaesthesia are rarely to be found except in abnormally suggestible individuals in whom they have been implanted by the observer himself. He holds the same of Mackenzie's areas of deep referred tenderness. He states that 'MacBurney's point is constantly found in appendicitis by those who believe in it, but rarely by those who do not . . .' It seems that in this particular instance hysteria claims two victims, the observer and the patient, but whether those who find it or those who do not are to be regarded as the subjects of suggestion would form an interesting thesis for discussion. In either case it is somewhat disturbing to contemplate the profound distrust of clinical methods which might be induced in the impressionable clinician if considerations of this kind obtained undue weight.

Those with surgical or general experience in the actual theatres of war will probably regard the statement that organic disease or injury is the most common source of suggestion of hysterical symptoms as too sweeping, for it has been frequently noted that men wounded in action were less prone to the development of hysterical manifestations than those who were merely concussed, 'blown-up', or only emotionally disturbed. Undoubtedly the perpetuation of disabilities arising from organic injury was most commonly seen in the home hospitals, but a special hospital, from its remote position, as well as from its selective character, is scarcely favourable to the forming of general conclusions on this point.

Great stress is laid upon the occurrence of an hysterical element in organic nervous disease and upon the importance of detecting and treating this. That there is often a pronounced functional element in such diseases as disseminated sclerosis and in tabes dorsalis with severe ataxy is an old and familiar observation, but neurologists will be inclined to demur to the statement that 'nothing but actually trying psychotherapy can show whether the whole incapacity is due to the organic disease or whether an hysterical and therefore a curable element is present'. As unequivocal evidence of organic nervous disease Hurst will accept only visible changes in the optic disk and cerebrospinal fluid, the absence of knee- and ankle-jerks, the extensor plantar response, the Argyll-Robertson pupil, a grossly irregular and eccentric fixed pupil, and the reaction of degeneration.

Under such conditions what are we to think of paralysis agitans, so recently promoted to the ranks of the organic diseases, now that all its physical signs are placed upon an *index expurgatorius*? Were the old authors right after all in describing it as a neurosis? This is a question that psychotherapy may be expected soon to settle for us.

Among views which the war can scarcely be said to have taught us about hysteria, we find it stated in Hurst's paper that the pernicious vomiting of pregnancy is hysterical, can easily be cured by psychotherapy, and should never necessitate the induction of labour. No evidence is forthcoming that this view has ever been put to any adequate test, and mercifully it is not likely to be received with enthusiasm until it becomes something more than an ingenious and hazardous speculation. Hurst continues that 'every woman knows that she is likely to vomit when she becomes pregnant, and the presence of other evidence of pregnancy may suggest vomiting'. What must we say of the woman who is first made aware of her condition by nausea or vomiting? Should we suspect her of an hysterical pseudocyesis? However, in such a case there would be an interval of several months in which to test the value of psychotherapy before the unmistakable signs of labour and delivery set our doubts at rest. It only remains for some one to suggest that abortion is due to claustrophobia in the foetus and may be averted by the prompt exhibition of psychotherapy *secundum artem*.

The value of the emphatic restatement of the doctrine that an hysterical element may overlie and exaggerate the disability due to organic disease, and that the observer may by suggestion endow his patient with certain physical signs is clear. For, as Hurst maintains, it is certainly apt to be forgotten. Nevertheless it may be over-emphasized and it would almost seem from his paper as though Hurst would place all clinicians into one or other of two classes: either into a very large group which is to be regarded as containing the unknowing inhabitants of a fools' paradise of auto- and hetero-suggestion; or, less probably, into a very small group of acute persons who, like modern witch-doctors, 'smell out' hysteria in their patients in a manner reminiscent of the tales of Rider Haggard.

It would be very difficult to make a general statement as to what we have learned about hysteria from the war that would command wide acceptance. What some regard as new, others would variously consider as a rediscovery, as mere speculation, or as frank error. In this, as in other respects, the war has made as many problems as it has resolved. If the reader will turn to the introduction to a charming review on hysteria written in 1911 by Kinnier Wilson (*Brain*, **33**, 293) he will find that the spirit of enthusiasm which hysteria has always inspired and the perennial rediscoveries of its cause and mode of removal characterize recent writings to no less a degree and are expressed with no less conviction than in those of a past generation, and he may be excused if he concludes with that admirable psycho-analyst King Solomon that there is nothing new under the sun—in this subject, at least. F. M. R. W.

F. R. Miller. The cortical paths for mastication and deglutition. *J. Physiol.*, 1920. **43**, 473.

Miller reviews the observations of Rethi (1893), who found that movements of mastication and of deglutition were obtainable on appropriate cortical stimulation in the rabbit. Stimulation of the infracortical path as far back as the plane of the subthalamic region also produced these movements, but behind this plane only steady jaw closure could be obtained, from which Rethi concluded that within or immediately below the thalamus there must be a centre for these movements. Miller's investigation was directed to obtain further information on the paths concerned. He found that stimulation of the cortex or of the subcortex as far back as the plane of the corpora mammillaria evoked rhythmical movements of mastication and of deglutition. When the mandible was divided in the mid-line it was seen that the masticatory movements were bilaterally symmetrical from stimulation of a single hemisphere. Posterior to the plane mentioned only steady jaw closure was obtained, the other rhythmic movements ceasing completely. The reason appears to be that at this level the upper motor neurones concerned pass across to their appropriate nuclei as aberrant fibres, while the jaw closure is due to direct stimulation at the base of the skull of the mandibular nerve at its point of exit, and not to stimulation of the crus. There is no evidence of any masticatory centre in the thalamus, and the path concerned could be traced from the cortex through the lower part of the internal capsule to the medial part of the pes at the level of the corpora mammillaria.

Two points of interest arise in connexion with these observations; first, respecting the bilateral character of the movements obtained by stimulation of a single hemisphere. Sherrington has concurred in the view expressed earlier by Beevor and Horsley that bilaterally symmetrical movements are relatively rarely represented in a single hemisphere, and from the few recorded movements of this kind he is inclined to remove mastication. Secondly, in connexion with the hypothetical centres for articulation and mastication in the basal ganglia, believed in by some neurologists, these observations, like the majority of experimental results afford little evidence for the various functions attributed to these structures on clinical and pathological grounds. F. M. R. W.

Marie, P. et Foix, Ch. Paraplégie en flexion d'origine cérébrale par nécrose sous-épendymaire progressive. [**Paraplegia in flexion of cerebral origin due to progressive sub-ependymal necrosis.**] *Rev. neurol.*, 1921, i, 1.

Flexion contracture of a lower extremity from cerebral lesion is extremely rare, while paraplegia in flexion is unknown in these circumstances. A single case of this condition from a ponto-bulbar lesion has been described by Babinski, but we cannot regard this as cerebral in localization. Marie and Foix describe what they believe to be the first recorded case of paraplegia in flexion of cerebral origin with an anatomical confirmation.

The patient was a woman of 70 with a paraplegia of many years standing. There was flexion contracture of the legs, which retained but little voluntary power. There is no mention of involuntary flexor spasms. The knee-jerks were absent, and one ankle-jerk persisted in a diminished degree. The flexion reflex and the extensor response were present in both limbs, and there was a crossed extension reflex. The abdominal reflexes were absent.

The upper limbs and the muscles supplied by the cranial nerves were normal. There was inequality of the pupils, myosis, and defective light reaction. There was marked mental enfeeblement.

Macroscopic examination revealed an irregular rough-walled dilatation of the superior cornu of the lateral ventricle of both sides. This increase in size had been produced at the expense of the cerebral substance which was eroded. The direction of enlargement was such that fibres proceeding from the paracentral lobules alone had been encroached upon and destroyed. The essential lesion was a slowly progressive softening due to the growth and coalescence of small areas of necrosis beneath the ependymal lining of the ventricle: *progressive sub-ependymal necrosis.* No lesion was detected in brain-stem or in cord, except that in the latter in the thoracic and lower segments the pyramidal tracts were somewhat pale and diminished in volume.

Microscopically, diffuse cell changes were found throughout both hemispheres.

The conclusion to be drawn from this case, Marie and Foix argue, is that a pure lesion of pyramidal fibres can produce the clinical picture of paraplegia in flexion with its characteristic reflex phenomena.

There is a considerable amount of evidence that pure pyramidal system lesions result constantly in the extended type of paralysis of the lower limbs, and it may be doubted whether a chronic case of diffuse cerebral disease in a senile patient, showing the pupillary changes described, is ideal material for far-reaching physiological hypotheses. A clean lesion in an otherwise healthy brain would have been far more convincing. The superior longitudinal sinus syndrome of Gordon Holmes and Sargent more or less fulfilled this condition and invariably consisted of a spastic paraplegia of extended type.

The dissociation between cutaneous and tendon reflexes recorded here and originally described by Babinski as occurring in paraplegia in flexion, is, it has been pointed out, illusory, and for this reason: the tendon-jerks examined—knee- and ankle-jerks—are both jerks of extensor muscles physiologically considered; while the reflex movements so prominent are flexor phenomena. Now the extensors in paraplegia in flexion show no reflex activity of any kind, except occasionally a crossed extension entirely secondary to a flexion reflex. The flexors, on the other hand, show intense reflex activity included in which is constantly a brisk hamstring-jerk. It is not true, therefore, to say that the tendon-jerks are absent in this clinical form of paraplegia, but it is correct to say that the extensor group (including the plantar flexors) shows no reflex activity of any kind.

Lastly, there is considerable evidence (*Brain*, 1914, **37**, 269, and 1918, **40**, 1) that in addition to interruption of the pyramidal system a lesion of paths descending from the brain-stem from centres therein is an essential preliminary to paraplegia in flexion. F. M. R. W.

Wilson, Margaret. Non-medullated fibres in the spinal ganglia. *J. Physiol.*, 1920, **43**, 446.

In 1912, Ranson described non-medullated fibres in the spinal ganglia, but Winifred Parsons has recently stated that the fibres so described are neuroglial in nature.

The present paper records histological investigations confirming Ranson's observations and demonstrating anew the absence of neuroglia in the spinal ganglia. F. M. R. W.

Souques, A. Traumatisme cranien et Tuberculome cerebral. [**Skull injury and tuberculoma of the brain.**] *Rev. neurol.*, 1920, i, 69.

A woman of 23 came under observation for Jacksonian fits beginning in the left hand and for the general symptoms of cerebral tumour: headache, vomiting, and loss of vision. There was bilateral optic neuritis.

At the age of 13 she had received a severe blow over the right parietal region, producing a scalp wound, but no loss of consciousness. Headache had followed this, severe at first, but becoming trivial until two years before coming under observation, when during pregnancy it had become severe again. After delivery fits developed and increased in frequency until she sought advice at the Saltpêtrière.

Operation revealed great thickening of bone under the old scar; decompression was performed, but she died three weeks later. At autopsy the dura was found adherent over a small area to the subjacent hemisphere in the right parietal region. At this site the pia-arachnoid was thickened over an area the size of a five-franc piece. Immediately beneath this lay a large solitary tubercle the size of a tangerine orange in a pocket between the rolandic cortex in front and the post-central convolution behind. It had apparently originated in the pia of the fissure of Rolando. It was very lightly adherent to the subjacent cortex and was readily enucleated. Histological examination confirmed the view that it was a solitary tubercle.
F. M. R. W.

Dickson, E. C. Botulism: a clinical and experimental study. *Monographs of the Rockefeller Institute for Medical Research*, 1920, **8**.

In view of the interest recently aroused in this condition from its passing identification with the disease now known as lethargic encephalitis, the clinical and pathological investigation recorded in this paper, the most recent on botulism, is noteworthy.

This investigation arose out of an outbreak in December 1913, in which twelve students were poisoned at a club banquet. The clinical picture of their illness was in all respects identical with that of botulism, and the article of food incriminated was a salad prepared from canned beans. However, the organism was not recovered from the one fatal case, while of the salad none remained to examine.

Later, several small outbreaks arising from the consumption of canned fruit or vegetables were studied.

Dickson summarizes the clinical picture as follows: the onset is usually from 18 to 24 hours after eating the poisonous food, but may be delayed for two or more days. The onset occurs with headache, giddiness, and general weakness and a sense of profound fatigue. There is no severe gastro-intestinal disturbance, though transient vomiting and diarrhoea are seen in some cases. The vomit is yellow and intensely bitter. Commonly, constipation of a most intractable form sets in at once, or after the transient purgation. The symptoms of cranial nerve paralysis appear early, all the motor nerves being involved. The third nerve is particularly early affected, producing dilatation and immobility of the pupils, which may be unequal and irregular in contour. There is ptosis, squint, diplopia, and sometimes nystagmus. The sixth nerve is very frequently involved, the fourth less often. There is unilateral or bilateral facial paresis and this with the ptosis gives the patient a peculiarly heavy, stupid expression.

The musculature of the soft palate, larynx, and pharynx are also affected, so that there is regurgitation of fluids through the nose, nasal voice, difficulty in articulation and in swallowing solids, which may enter the air passages. A persistent ineffectual cough is a very distressing symptom. The mucosa of the mouth and pharynx is dry and secretes a thick stringy mucus, which the patient finds it difficult to expel.

There is no true paralysis of the muscles of the limbs and trunk, but rather a progressive general asthenia and hypotonus, to which ataxy of movement may be added. As a rule the tendon reflexes persist, though their absence is not unknown, and the cutaneous reflexes are also usually preserved. The plantar reflex is not specifically mentioned. Sensory disturbances are said to be absent.

On the visceral side there appears to be a general inhibition of secretion from the skin and mucous membranes, though the quantity of urine may be normal. Even this, however, is subject to wide variations in different cases. In the outbreaks investigated the pulse-rate was rapid and the temperature subnormal until death, unless pulmonary complications set in. Respiratory failure is the cause of death and in the later stages of the illness there is severe dyspnoea. The disease is rendered more distressing by the fact that the patient retains full mental power to the last. The majority of cases die in from four to eight days, and in those that recover convalescence is extremely slow and tedious, though no permanent paralytic sequelae remain.

In the United States the mortality in recent outbreaks is 64 per cent.

The first pathological examination of the nervous system of a human victim of the disease is attributed to Paulus (1915), who described the condition as a polioencephalitis superior and inferior with an acute degenerative haemorrhagic lesion. To the naked eye there were in his case multiple minute haemorrhages in the brain, particularly in the grey matter round the cerebral ventricles, in the basal ganglia, and in the floor of the fourth ventricle. Microscopically, there was intense vascular congestion with haemorrhages from the vessels most marked in the brain-stem and basal ganglia. There was no inflammatory reaction, and no perivascular infiltration with round cells. In the affected region, the nerve cells showed various grades of acute degenerative change, and in this the ganglion cells of the cervical cord were involved.

In the fatal case of the Stanford University student mentioned earlier, Ophüls (*Arch. Int. Med.* 1914, **14**, 589) found broncho-pneumonia and widespread congestion of the viscera. There were no macroscopic haemorrhages, but widespread congestion of the brain with thrombosis of arteries and veins of meninges and brain. The brain-stem was most severely affected and showed numerous minute thromboses and haemorrhages. In the nerve cells, there was no discoverable change and their Nissl granules are said to have been intact.

The paper also contains an historical introduction, a review, and a critical summary, and an account of a large series of experimental observations with *Bacillus botulinus* and its toxin. These sections have not been dealt with in this abstract. F. M. R. W.

Scripture, E. W. The nature of epilepsy. *Proc. Roy. Soc. Med.* (*Section of Psychiatry*), 1920, **13**, 18.

By the graphic recording of the vibrations transmitted by the voice to the flexible membrane of a tambour, and the plotting and measuring of the records, Scripture obtains 'melody plots' of the speech in health and in various nervous diseases. He finds that throughout the varying inflexions of the voice that appear on the record there are seen finer fluctuations in the curves, and these constitute the flexibility of the melody. The records in epilepsy show an absence of this flexibility, and to the experienced ear the speech of the epileptic is wooden and expressionless. Thus, Scripture claims to be able to identify the epileptic child in a hospital ward by its 'Good morning' greeting.

Far-reaching practical results and theoretical conclusions are said to follow from these tenuous observations; they can be indicated only by quotations from the original paper. Thus, 'During the war many men came to me with stories of fits in order to secure certificates of exemption from service. More than one had been carefully trained to tell a story that was typically epileptic. Although relatives and witnesses might be brought, my final judgement on the genuineness of the case was based largely and sometimes entirely on the melody of the patient's speech. If the patient did not have the typical epileptic inflexibility, I could not bring myself to believe him to be a genuine case,' and again, 'for purposes of differential diagnosis (i. e. from hysteria) this inflexibility of epileptic speech is perhaps more to be relied upon than an actual fit.'

On the theoretical side we read that 'the inflexibility, or woodenness, of the epileptic melody may perhaps be the expression of some peculiarity of the epileptic character'. The argument is then taken up by Pierce Clark, who is quoted as saying that 'the very essence of the epileptic character is an emotional attitude of a stubborn unyielding demand that the environment shall conform precisely to the person's wishes', and that 'the epileptic seizure is a reaction to the strain of an intolerable environment by a lapse into unconsciousness'. Scripture rounds off the tale by supposing that 'the inflexibility of the epileptic melody would be an expression of the epileptic's attitude towards his environment.'

Here, as in many recent contributions to the study of neurological problems, we see the accumulated clinical experience of generations lightheartedly jettisoned and some special personal method, attainment, or fanciful theory exalted into the first place in the diagnosis and treatment of disease.

This is the more open to objection when, as in the present instance, an extravagance of speculation is based upon a similitude of the scientific method.

Those who hold the traditions of the clinical method in some reverence will view this latest expression of the new spirit in dealing with the problems of clinical neurology with bewilderment and apprehension.

For those who cannot accept his revolutionary attitude, Scripture has himself indicated a method by which it may be met. He says that 'when the epileptic's mind finds the demand on it too great, it puts out the sign "Not at home"'. F. M. R. W.

Dusser de Barenne, J. G., and **Magnus, R.** Beiträge zum Problem der Körperstellung. III. Die Stellreflexe bei der grosshirnlosen Katze und dem grosshirnlosen Hunde. [**Studies in orientation. III. The positional reflex in decerebrate cats and dogs.**] *Arch. f. d. ges. Physiol.*, 1920, **180**, 75.

Magnus has extended his observations on decerebrate rabbits. He found that there were four groups of reflexes which determined position. These were: (1) the labyrinth position; (2) the body position in relation to the head; (3) the neck position; (4) the body position in relation to the body. In the intact rabbit it was shown that the animal had no other positional reflexes which were not found in the decerebrate animal. The eyes played no part. The results of the experiments with dogs and cats showed that the decerebrate animals possessed the same reflexes as the intact rabbit. There are no additional reflexes. C. G. L. W.

de Kleijn, A. and **Magnus, R.** Beiträge zum Problem der Körperstellung. IV. Optische Stellreflexe bei Hund und Katze. [**Studies in orientation. IV. Optical positional reflexes in dogs and cats.**] *Arch. f. d. ges. Physiol.*, 1920, **180**, 291.

Decerebrate cats and dogs have the same four positional reflexes as rabbits. In the air they rely almost exclusively on the labyrinth and the closely connected neck reflex. If both labyrinths be extirpated they have no sense of position. In fact, cats and dogs use the eyes to determine position. After extirpation of both labyrinths, dogs practically and cats in a high degree are incapable of determining position, but after a few days learn to use the eyes and are able then to bring themselves into the normal position. The optical reflex is connected with an intact cortex. The optical reflex is only used vicariously when the labyrinthine reflex is abolished.

C. G. L. W.

PATHOLOGY AND BACTERIOLOGY

Ledingham, J. C. G. Dysentery and enteric disease in Mesopotamia from the laboratory standpoint. An analysis of laboratory data during the eighteen months ending Dec. 31, 1918. *J. Roy. Army Med. Corps*, 1920, **34**, 189.

Col. Ledingham, who, during the war, visited Mesopotamia as a member of the Medical Advisory Committee, and who later acted as Consulting Bacteriologist to the Mesopotamian Expeditionary Force, presents in this paper an analysis of laboratory findings in dysentery and enteric disease brought into relation with the incidence figures for the area as a whole and its chief parts. By the adoption of a laboratory return which rendered the data in a form amenable to statistical treatment, it was possible from month to month to form an estimate of the actual incidences of amoebic and bacillary infections in relation to the total dysentery incidence. Charts are constructed which show at a glance the total incidence of dysentery and diarrhoeal disease over the period in question, and the proportion of that incidence attributed by the laboratory returns to amoebic and bacillary injection both in British and in Indian troops.

Two distinct waves of dysentery and diarrhoeal diseases occurred in the course of the Mesopotamian year, a spring wave commencing in late March or early April which reached its maximum in May, and an autumnal wave commencing in late September or early October with a maximum in November. January, February, and March were the months of minimal incidence.

A chart is submitted to show the waves of the fly prevalence in relation to those of dysentery and diarrhoeal disease. The correspondence in time of the two prevalences is, as the writer points out, remarkably close, but attention is drawn to the fact that while flies all but disappear during the hottest months of the year (July and August) there is no corresponding reduction of the dysentery incidence. The maintenance of the dysentery incidence during this period at a level not inferior to that of April is attributed by the author to distributing factors, other than flies, operating in a population containing a large quota of chronic and carrier infection remaining over at the close of the spring wave.

The incidence of dysentery was very much higher in British than in Indians, as the following figures show:

Minimal incidence in British (February)	10·9 per 10,000
,, ,, ,, Indians ,,	5·6 ,, ,,
Maximal incidence in spring wave, British (May)	59·6 ,, ,,
,, ,, ,, ,, Indians ,,	17·2 ,, ,,
,, ,, ,, autumnal wave, British (Nov.)	85·3 ,, ,,
,, ,, ,, ,, Indians ,,	21·9 ,, ,,

The incidence of amoebic dysentery throughout the year followed very closely the variations exhibited by the total dysentery incidence and accounted in British troops for 20–30 per cent. of that incidence.

In the forward area during the epidemic waves, the amoebic percentage in British troops fell to 5 or 10 per cent., and laboratory investigations showed clearly that in epidemic seasons bacillary infections formed the great majority of the acute dysenteries. Under the best conditions for securing high returns of *B. dysenteriae* isolations, such as prevailed at Bagdad in connexion with evacuations from the forward area, it was possible to demonstrate the bacillary origin of 50–60 per cent. of the acute dysenteries submitted to the bacteriological investigation. Of 715 isolations of *B. dysenteriae* in British troops, *B. Shiga* was recovered in 45·3 per cent., and *B. Flexner* in 54·7 per cent. In the early stages of the spring and autumn epidemics it was noted that *Shiga* infections predominated, to be replaced during the declining stages and in the epidemic-free intervals by *Flexner* infections accompanied by a considerably lower mortality rate.

Atypical, i.e. inagglutinable, dysentery strains of the mannite-fermenting type were on the whole infrequent, possibly by virtue of the polyagglutinating capacity of the Lister Institute *Flexner-Y* sera employed for diagnosis throughout the area.

With regard to enterica, the specific diagnosis of 'T', 'A', and 'B' infections was dependent entirely on isolation results, and every effort was made to increase the total of bacteriologically confirmed cases in relation to the unconfirmed or 'Clinical Enteric Group' (E. G.) cases.

Of 1,574 notified cases of enterica which occurred in the Forces during the 18 months under review, 734 or 46·6 per cent. were confirmed by isolation of the infecting organism.

A series of 381 confirmed British entericas yielded 123 'T', 218 'A', and 40 'B' infections, while 303 confirmed Indian entericas yielded 158 'T', 97 'A', and 48 'B' infections.

Enteric fever was therefore more prevalent relatively to paratyphoid infections among Indian than among British troops.

Copies of the laboratory forms used in the area appear as appendices to the paper. J. C. G. L.

Laybourn, R. L. The fermentation of polysaccharids by *Bacillus aerogenes*. *J. Infect. Dis.*, 1920, **26**, 418.

The differentiation of *coli*-like bacteria into two subgroups by the Voges-Proskauer and methyl-red reactions seems to be well established, and correlated with habitat. The *B. coli* group (Voges-Proskauer negative—methyl-red positive) is characteristically faecal in origin, whereas the *B. aerogenes-cloacae* group (Voges-Proskauer positive—methylene-red negative) predominates in soil and on grain, but it is relatively infrequent in faeces as voided, although common in the upper levels of the intestine in man. Under certain conditions, however, it may constitute a considerable proportion of the intestinal *coli*-like flora. The present research was undertaken to determine whether there are differences between intestinal *B. aerogenes* and that found in soil. Altogether, 49 strains of *B. aerogenes*, from a variety of sources, were tested on a large number of different starches obtained from arrowroot, barley, bean, corn, oat, rice, rye, sago, and other substances, as well as on inulin, glycogen, and hemicellulose. Forty-six of the strains of *B. aerogenes* fermented all the starches employed, with gas formation; 3 produced gas in inulin, 3 in glycogen, but none attacked date-seed hemicellulose. Of the 3 strains which did not produce gas in all the starches, one failed to attack the starch of beans and ginger, another failed to ferment the starch from lentil, oat, and wheat, while the third produced a small quantity of gas in the starches from corn, tapioca, and wheat only. The interesting fact that micro-organisms which fermented one starch usually fermented all the others, would indicate either that the same enzyme was capable of breaking down all of them, and that starches are polymers, or that the microbe produced a multiplicity of enzymes. It was noted that although all the starches were attacked there was a marked difference in the hydrogen-ion concentration produced with different starches. The results also tended to show that *B. aerogenes* does not hydrolyse starch through the usual series of compounds, erythrodextrin, achro-odextrin, maltose, glucose. It has generally been supposed that *B. aerogenes* produces acetyl-methyl-carbinol (Voges-Proskauer reaction) from glucose, and this was the case with the cultures studied by the author. When, however, acetyl-methyl-carbinol was looked for in the starch-fermented cultures, it was not found, which, in the opinion of the author, indicated that the decomposition of the starch did not progress to the glucose stage before assimilation by *B. aerogenes*. It did not appear that starches could be usefully employed to differentiate the source of origin of strains of *B. aerogenes*.

W. B.

Maymone, B. Variazioni biologiche del *B. Shiga*. Osservationi nel corso di un' epidemia di dissenteria bacillare. [**Biological variation of *B. Shiga* observed during an epidemic of bacillary dysentery.**] *Ann. d'ig.*, 1919, **29**, 653.

The Shiga Kruse bacillus was isolated during an outbreak of dysentery in a barrack. In the course of his investigation the author had occasion to study all bacilli that are Gram-negative, non-motile, non-lactose fermenters, and do not liquefy gelatin. He observed that in the same stool microbes were isolated which showed some difference either biologically or serologically. But these differences, according to the writer, are not of such importance as to lead to the establishment of new species, as it is very often done. They are variations which have arisen from the interaction between the fluids of the human body and the microbes of the intestinal tract. Thus, for example, he studied 2 strains (53 and 53-bis) isolated from the same patient. No. 53 was a typical *Shiga*, 53-bis did not ferment glucose. Moreover, 53 was agglutinated by *Shiga* serum, whereas 53-bis was not. On the other hand the antiserum for 53 agglutinated in the same dilutions both 53 and 53-bis.

The author came to the conclusion that the individualization of a species on serological or fermentative grounds alone was erroneous, and in order to arrive at the identification of a dysenteric bacillus the pathological changes produced in rabbit must be taken into consideration, for the anatomo-pathological changes presented by this animal is the most constant character observed.

A. D.

Kabeshima, T. Thérapie expérimentale des porteurs de germes. [**Experimental therapy of 'carriers'.**] *Compt. rend. Acad. d. Sc., Par.*, 1920, **170**, 71.

The author has observed that 1 c.c. of the autolisate of the d'Herelle 'microbe' injected into the vein of a rabbit gives to the bile of the latter a bactericidal power against *B. Shiga* after 12 to 24 hours.

On the above experiment Kabeshima bases the treatment of carriers. He first of all tries to make a rabbit a carrier, by injecting into its gall-bladder $\frac{1}{20}$ of a loop of 24 hours' agar culture of *B. Shiga*, then he inoculates such rabbit carriers with the d'Herelle autolisate for treatment purposes.

Four series of experiments were made which are given below :

(1)	1	animal	injected—	2	injections	of	5	c.c.	in 24 hrs.	interval—	1	control
(2)	2	,,	,,	3	,,	,,	5	,,	,,	,,	2	,,
(3)	5	,,	,,	5	,,	,,	1	,,	,,	,,	5	,,
(4)	4	,,	,,	7	,,	,,	1	,,	,,	,,	4	,,

In the series 1 and 2 the controls as well as the injected animals showed Shiga on culture from bile.

In series 3 and 4 all the injected animals presented sterile bile, whereas the controls showed Shiga bacilli.

A. D.

Takenouchi, M. Sensitized and non-sensitized vaccines in cholera immunization. *J. Infect. Dis.*, 1920, **26**, 441.

The author carried out a number of experiments on guinea-pigs and rabbits to determine whether sensitized cholera vaccine was as effective or more so than ordinary non-sensitized dead cultures in equivalent doses. During the contact of the culture with the immune serum in the process of sensitization he found, as others have done, that the toxicity of the culture is greatly reduced. This diminished toxicity is caused not only by the washing but also by the action of the anti-cholera serum on the toxic substances of the cholera vibrios. The author emphasizes the difficulties in determining the value of the vaccine on account of the variations which may occur in different cultures of one and the same cholera vibrio. By careful determination of the lethal dose and the utilization of twice this quantity within 3–5 hours after the intraperitoneal inoculation of the respective vaccines, he was able to determine that non-sensitized cholera vaccine is markedly superior to sensitized vaccine in protecting the lives of guinea-pigs subsequently inoculated with living virulent cultures. Further, non-sensitized cholera vaccine produces, in the serum of rabbits, a greater bacteriolytic content than sensitized vaccine. Inoculated subcutaneously, non-sensitized cholera vaccine is much more effective than a similar sensitized vaccine. W. B.

Cantacuzène, J. La pathogénie du choléra et la vaccination anti-cholérique. [**The pathogenesis of cholera and anti-cholera vaccination.**] *Ann. de l'Inst. Pasteur*, 1920, **34**, 57.

A long and detailed work on the personal experience gained by the author in the various theatres of war during the years 1914–1916. High doses, 3 to 4 milliards, of dead microbes, are necessary to produce a solid immunization. In cases of outbreaks the only means to arrest the spread of the disease is vaccination. It is necessary to vaccinate during and in the midst of an epidemic, neglecting to take into account the negative phase. He is of opinion that the immunity arises in the intestine before appearing in the blood. A. D.

Jordan, E. O. The differentiation of the paratyphoid-enteritidis group. Irregular and variable strains. *J. Infect. Dis.*, 1920, **26**, 427.

This is a study of 14 strains of bacteria, of the paratyphoid-enteritidis group, which showed irregularity and variability in cultural and agglutination reactions tested at different periods. The details should be consulted in the original. A comparison of the published results of others together with his own observations led the author to the conclusion that variations both in nature and in artificial cultures are exceedingly common in the paratyphoid-enteritidis group. At times there seems to be a special tendency to variation and a number of varieties may split off from the parent stock. Such outbursts, in the opinion of the author, suggest the possibility of conjugation phenomena rather than the direct action of environment.

W. B.

Cannon, P. B. ***Bacillus enteritidis*** **infection in laboratory rats.** *J. Infect. Dis.*, 1920, **26**, 402.

This is a study of an epizootic of enteritis in rats, 45 of which died out of a total of 52 during a period of four weeks. A paratyphoid organism was isolated from the heart blood from 31 out of 35 examined. Cultures showed gas in glucose, maltose, levulose, galactose, mannitol and dulcitol, but none in lactose, saccharose, dextrin, inulin or salicin. In three or four days milk was markedly alkaline. Agglutination tests showed the organism to belong to *B. enteritidis* which was pathogenic when introduced subcutaneously, intraperitoneally or *per os*. It was believed that the infection was mainly spread by flies. *B. enteritidis* was also obtained from two fleas from the affected rats. The literature of similar epizootics in rodents is given. W. B.

Caprone, G. Osservazioni sull' agglutinabilità di alcuni microorganismi coltivati in terreni acidi ed alcalini. [**Observations on the agglutinability of certain microbes cultivated in acid and alkaline media.**] *Sperimentale, Arch. di biol.*, 1919, **73**, 384.

B. typhosus and *B. paratyphosus* cultivated in acid media (acidified with HCl and of a concentration HCl $\frac{N}{40}$) grow very slightly at first, but after a certain number of passages on the same media they grow readily. The cultures thus obtained are agglutinated in higher dilution than those obtained on the usual media. The same organisms grown on alkaline media (NaOH $\frac{N}{40}$) are agglutinated in lower dilution than the control, because according to the author the alkali splits the agglutinogenic substance. A. D.

Matsunami, Toitsu. Studies on the meningococcidal activity of blood. *J. Immunol.*, 1920, **5**, 51.

The author studied the phenomenon of destruction of meningococci by the bactericidal substances in the serum or blood of normal and immunized rabbits. The technique employed was that recommended by Heist and was carried out with modified Wright's pipettes. The blood and serum of normal rabbits exert a definite bactericidal action *in vitro* and this property in the case of the *blood* may be increased to a certain extent by injection of living or autolysed cultures. The author was unable to demonstrate an increased bactericidal content in the *serum* of immunized rabbits. W. B

Idzumi, G. Experimental pneumococcus meningitis in rabbits and dogs. *J. Infect. Dis.*, 1920, **26**, 374.

The extreme fatality of pneumococcic meningitis in man led the author to study the conditions under which a pneumococcic inflammation of the meninges can be set up experimentally in dogs and rabbits. Three strains of pneumococci were employed, two of which had produced meningitis in man. It was found that simple intravenous inoculation of the living virulent cultures did not cause a localization in the meninges. Intravenous inoculation followed by spinal puncture and the subthecal injection of sterile broth or serum was usually followed by the development of acute meningeal congestion and sometimes of a suppurative leptomeningitis. Similar experiments in dogs invariably caused acute congestion but without suppuration. Subthecal injections of pneumococci into the lumbar region in rabbits were usually followed by a fatal suppurative leptomeningitis with symptoms of hypersensitiveness, opisthotonus, and convulsions, death usually occurring from the second to the fifth day. Spinal puncture on the second day usually showed that the cerebrospinal fluid was turbid and contained large numbers of polynuclear leucocytes and diplococci, the latter being mainly extracellular. Cultures from the heart blood invariably showed pneumococci. In similar experiments with dogs, meningeal irritation and actual suppurative leptomeningitis were produced, but with much less regularity and only as a result of the injection of large doses of pneumococci. After death, cultures of the spinal fluid were mostly positive, whereas cultures from heart blood were generally sterile. W. B.

Thomsen, Oluf and **Wulff, F.** Septicémie méningococcique. Cultures prélevées des pétéchies. Cause pathogénique des taches pétéchiales. Type du méningocoque. [**Meningococcic septicaemia. Cultures obtained from petechiae. Cause of petechiae. Type of the meningococcus.**] *Compt. rend. Soc. de biol*, 1920, **83**, 701.

The authors emphasize the severity of epidemics of cerebrospinal meningitis in Denmark, since 1917, consisting as they did of septicaemia with rashes of a papular or spotted type. In a number of cases the cerebrospinal fluid was clear and completely devoid of meningococci. Death sometimes occurred as early as 24 hours. In the cases in which there were no meningeal symptoms the diagnosis was made from blood cultures or more frequently from the petechial spots. A small area including a spot was excised during life or after death, and from the lower surface material was inoculated on ascitic agar in plates. Using Pappenheim's methyl green-pyronine stain, the authors found that in sections the meningococci were frequently found inside cells placed along the wall of the vessels. The lumen of the latter was also frequently occupied by cells, endothelial or leucocytic, packed with meningococci. The cocci isolated were tested for agglutination and absorption reactions by means of Gordon's type sera. All the cocci tested conformed to a type which the authors designate as A, and which was not identical with any of Gordon's types. W. B.

Prell, H. Zur Aetiologie der pandemischen Grippe. [**The aetiology of pandemic influenza.**] *Ztschr. f. Hyg. u. Infektionskrankh.*, 1920, **90**, 127.

In this long paper the author reviews the aetiology of influenza as it appears to German workers, and especially the work relating to filter-passing organisms. He himself described certain granules in sections of pneumonic lungs which he had stained with iron-haemotoxylin, and upon these bodies he bestowed a name indicating their rôle as the cause of influenza.

He now seeks to produce some justification for his assumptions and, although he persistently throughout describes his granules as the cause of influenza, he finally concludes that the matter requires further investigation.

The paper does not require extended notice. P. F.

Prein, F. Zur Influenzapandemie 1918. [**The influenza pandemic of 1918.**] *Ztschr. f. Hyg. u. Infektionskrankh.*, 1920, **90**, 65.

The author was responsible for bacteriological, pathological-anatomical and epidemiological studies of the civil and military population of Mecklenburg-Schwerin.

His accounts of the autopsies are similar to those of others. His bacteriological work also establishes the presence of, chiefly, haemolytic streptococci, pneumococci, staphylococci and other bacteria. For the growth of *B. influenzae* he made use of plain sheeps' blood-agar and failed to find this organism except in an unimportant percentage of cases. He is of opinion that his medium is as good as those of others.

Reviewing the literature (exclusively German) he points out that equally experienced bacteriologists have failed to find the bacillus or have found it in a large number of cases; therefore questions of technique cannot arise and the variation must depend upon an unequal geographical distribution of the organism. This is inconsistent with the view that *B. influenzae* is the cause of influenza as is the occurrence of the organism in non-influenzal diseases. According to him influenza is due to an unknown virus situated primarily in the mucous membranes at the lower end of the trachea. It causes a catarrhal inflammation, lowers the resistance and makes way for the invasion of streptococci or of *B. influenzae.* The latter is a secondarily infecting micro-organism. He is opposed to 'filter-passers' having any connexion with the disease.

The author's chief objection to *B. influenzae* depends upon his view that if two bacteriologists of equal reputation obtain different results in an investigation, they must both be right. This, however, seems illogical. It may be mentioned that, although he obtained equally good results with sheeps' blood-agar and Levinthal's medium, others of equal repute find a great difference in the values of these two media.

It will be noticed that this work emanates from an institute of which 'Prof. Pfeiffer' is Director. This is not Richard Pfeiffer, the discoverer of *B. influenzae.* P. F.

MALONE, R. H. and **McKENDRICK, A. G. Evidence regarding the immunity conferred by an attack of influenza, with a study of three local epidemics.** *Indian J. M. Research*, 1919, **7**, 372.

Statistics relating to an epidemic of influenza in July 1918 and November 1918 in three different communities in Calcutta were analysed. The results strongly suggest that immunity is acquired by one attack of influenza and that it lasts at least nine months. Another point brought out by a study of these epidemics is the remarkably rapid progress of the disease and its almost as rapid decline.

In an appended mathematical note by Major A. G. McKendrick, he points out that the problem contained in the above statistics is of the same type he has dealt with in previous papers in the *Indian Journal of Medical Research* (vol. 2, p. 882; vol. 3, pp. 266, 271, and 667).

Let ν_x denote the number of persons who have suffered from x attacks, then for variations in ν_x during the time dt we have

$$dv_x/dt = \partial_{x-1}\nu_{x-1} - \partial_x \nu_x,$$

where ∂_x is the probability that an individual, who has suffered from x attacks, may experience a further attack. It is assumed as an approximation that $\partial_x = b - cx$ (see *Proc. Lond. Math. Soc.* Feb. 1914), and the equation has for solution

$$v_x = N\frac{b}{c}\left(\frac{b}{c}-1\right)\dots\left(\frac{b}{c}-x+1\right)\frac{\left(\frac{\mu}{\nu}-1\right)^x}{x!}\left(\frac{\nu}{\mu}\right)^{b/c}.$$

Here N is the total population, μ is the mean number of attacks per individual, b and c are constants, v is the square of the standard deviation, and $c/b = \frac{v-\mu}{\mu^2}$. The above-mentioned statistical values are then substituted in these equations, and it is found there is a close agreement between the observed and calculated values. It is concluded that these groups of statistics are consistent with the view that a high degree of immunity supervened on the first attack. W. A. M. S.

McKendrick, A. G. and **Morison, J.** **The determination of incubation periods from maritime statistics, with particular reference to the incubation period of influenza.** *Indian J. M. Research.*, 1919, **7**, 364.

The authors seek by mathematical calculation to determine the number of days, after leaving port, on which the first case of influenza appeared. They base their reckonings on a pamphlet published by the Director of Quarantine of the Commonwealth of Australia, giving the records of observations on the incidence, spread, and decline of epidemics on board ships. They show how it is possible to deduce the mean period of incubation and also the expected frequency of occurrence of all incubation periods. The following is a synopsis of the mathematical argument adopted, it being assumed that in each ship only a single case of influenza was taken on board. The validity of this assumption is afterwards examined by statistical grouping and found to be correct.

'Probability' here means that a case showed symptoms on any particular day, irrespective of whether the patient did or did not show symptoms on the previous days.

Let p_r be the probability that a case showed symptoms on the r^{th} day, so that $1-p_r$ is the probability he did not show symptoms on that day. The probability that the patient had an incubation period of r days is $Z_r = (1-p_1)(1-p_2) \ldots (1-p_{r-1})\,p_r$, where Z_r denotes this probability.

Now the probability of a first case occurring on any particular day is the sum of the probabilities of the ways in which it can occur on that particular day, divided by the sum of the probabilities of the ways in which it can occur on all the days. Hence the probability of occurrence of a first case on the r^{th} day is $\frac{Z_r + Z_{r+1} + \ldots}{\Sigma r\,.\,Z_r}$.

The frequencies of occurrence, where N is the total number of infected ships, and only a single case was taken on board, are

$$F_1 = N(Z_1+Z_2\ldots)/\Sigma r\,Z_r, \qquad F_2 = N(Z_2+Z_3\ldots)/\Sigma r\,Z_r,$$
$$F_3 = N(Z_3+Z_4\ldots)/\Sigma r\,Z_r, \qquad F_4 = N(Z_4\ldots)/\Sigma r\,Z_r,$$

which, since the sum of the probabilities of all possible incubations is certainty, become

$$F_1 = N/\Sigma r\,Z_r = 64, \qquad F_2 = N(1-Z_1)/\Sigma r\,Z_r = 17,$$
$$F_3 = N(1-Z_1-Z_2)/\Sigma r\,Z_r = 5, \qquad F_4 = N(1-Z_1-Z_2-Z_3)/\Sigma r\,Z_r = 2.$$

Here the values 64, 17, 5, and 2 are obtained from the Australian statistics. Solving these for Z and inserting in

$$Z_r = (1-p_1)(1-p_2)\ldots(1-p_{r-1})\,p_r$$

we get the values of p. It is assumed as a first approximation that p_r is constant within the range of observation, so that

$$Z_r = p(1-p)^{r-1}; \quad \Sigma r\,Z_r = 1/p; \quad Z_r + Z_{r+1}\ldots = (1-p)^{r-1};$$

while $F_r = NZ_r$. The best value of p is obtained by moments. It is $p = N/\Sigma r\, F_r = 88/121 = 0{\cdot}727$. With this value we get $F_1 = 63{\cdot}98$ observed 64; $F_2 = 17{\cdot}47$, observed 17; $F_3 = 4{\cdot}77$, observed 5; $F_4 = 1{\cdot}30$, $F_5 = 0{\cdot}36$, observed 2. $Z_1 = 0{\cdot}727$, $Z_2 = 0{\cdot}189$, $Z_3 = 0{\cdot}054$, $Z_4 = 0{\cdot}014$ i.e. of 100 cases of influenza it is to be expected that 72·7 would have incubation periods of 1 day, 18·9 of 2 days, 5·4 of 3 days, and 1·4 of 4 days. The mean incubation period is 32·7 hours.

If the probability of a case being infective is related to the probability of symptoms being apparent, the initial period of non-infectivity in influenza must be of short duration. W. A. M. S.

JORDAN, E. O. and **SHARP, W. B. Influenza studies. I. Immunity in influenza.** *J. Infect. Dis.*, 1920, **26**, 463.

In spite of abundant opportunities for observation the question whether immunity is conferred by an attack of influenza has not been settled. To a certain extent this is no doubt due to the fact that 'influenza' is a clinical concept and as such is nebulous. It has been said that the relatively low incidence in elderly persons observed in 1918 was due to immunity acquired in the pandemic of 1889–90. The case rate per 1,000 living in 1918 in the age group 60–70 was apparently much lower than the case rate in the age group 35–45, although both groups were exposed presumably in equal degree in the 1889–90 pandemic. The authors made personal observations in connexion with about 6,000 young recruits in the Great Lakes Naval Training Station in the vicinity of Chicago, and in Camp Grant, Rockford, Ill. With respect to the first group consisting of 3,905 men, 1,112 (28·5 per cent.) gave a history of having had the disease in the 1918–19 epidemic, and 881 (22·6 per cent.) were again attacked in 1920. Of the 1,112 who had had influenza 236 (21·2 per cent.) had a repeated attack in 1920, while of 2,793 who had not had a previous attack, 645 (23·1 per cent.) were affected in 1920. In the Camp Grant series there were 2,472 soldiers of whom 390 (15·8 per cent.) had influenza in 1918–19 and 288 (11·7 per cent.) in 1920. Of the 390 men with previous influenza history, 61 (15·6 per cent.) were attacked in 1920, while of 2,082 who gave no evidence of having suffered in 1918, 227 (10·9 per cent.) were attacked in 1920. Taking the two series together we have the following figures:

Totals.	Number giving definite history.	Number that had influenza in 1920.	Percentage attacked in January 1920.
Number that had influenza, 1918–1919	1502	297	19·8
No history of influenza	4875	872	17·9

From these figures the authors infer that no marked immunity exists 12–15 months after a previous attack of influenza. They do not show that some degree of immunity may not obtain at an earlier period. W. B.

FILDES, P. and **MCINTOSH, J. The aetiology of influenza.** *Brit. J. Exper. Path.*, 1920, **1**, 119.

In this, the first part of a general review upon the aetiology of influenza, the authors discuss the grounds upon which a supposed pathogenic virus may be associated with the causation of an infective disease. The modern applications of 'Koch's postulates' are considered.

P. F.

Tunnicliff, Ruth. Observations on green-producing cocci of influenza. *J. Infect. Dis.*, 1920, **26**, 405.

The exact differentiation of the various cocci so frequently isolated during the influenza epidemic of 1918–19 has not been completed. After a careful analytical review of the existing literature, the authoress continuing her previous investigations (*J. Infect. Dis.*, 1918, **23**, 572; 1919, **24**, 181), now describes the characters of seven strains of Gram-positive cocci giving greenish colonies on blood-agar plates. They were isolated from the oedematous brains of cases of influenzal broncho-pneumonia. Only one of the strains was soluble in bile, but this culture was not agglutinated by pneumococcus sera of types I, II, or III. All seven fermented glucose, lactose, saccharose, and raffinose. Six fermented salicin, two inulin, and two mannitol. Morphologically the micro-organisms were usually lanceolate and capsulated. The serum of rabbits immunized with strains of cocci obtained from influenza cases contained opsonins and agglutinins for other similar bile-insoluble influenza cocci, and also for influenzal cocci which were bile-soluble and which were agglutinated by anti-pneumococcus sera, indicating that the green-producing cocci from influenza cases constitute a group the members of which are closely related immunologically. Absorption experiments confirmed this view. W. B.

Grace, Linwood G. and **Highberger, Florence** (1). **Acid production by *Streptococcus viridans* in mediums of different hydrogen-ion concentration.** *J. Infect. Dis.*, 1920, **26**, 451.

Grace, Linwood G. and **Highberger, Florence** (2). **Variations in the hydrogen-ion concentration in uninoculated culture medium.** *J. Infect. Dis.*, 1920, **26**, 457.

In connexion with their work on *Streptococcus viridans*, the authors have endeavoured to find out whether a medium of one reaction was superior to that of another for growing the above organism. They assume that the rate of acid production was a fair index of the rate of growth and vitality. The results indicate that growth will occur between P_H 6·4 and 8·0. Retardation was noted if the medium was more alkaline than P_H 7·6, and the most rapid growth was in a medium which had an initial reaction of P_H 6·8.

Between 5 per cent. ascitic broth, 0·2 per cent. glucose broth, and 1 per cent. glucose broth there appears to be no appreciable difference when growing a pure culture.

In their second paper the authors worked with uninoculated media, and noted their reactions before and after incubation. They found that the reaction was not as stable as they had supposed. The reactions varied from day to day and the final autoclaving produced a change. The factors producing these changes are probably the acid formed by the breaking up of glucose, or the amino acids from peptone, or possibly the absorption of CO_2.
W. A. M. S.

Havens, L. C. Biologic studies of the diphtheria bacillus. *J. Infect. Dis.*, 1920, **26**, 388.

The question whether different morphological types of diphtheria bacilli remain constant has never been satisfactorily determined. The present research was undertaken to determine whether variations in morphology and staining reactions occur, and, if so, under what conditions. An attempt was also made to determine the relation of the morphological forms to biological characters, such as virulence, toxin production, and agglutination. Strains, of diphtheria bacilli, to the number of 154 were investigated, the classification employed being that suggested many years ago by Wesbrook. It was found that the morphological types of Wesbrook show a tendency to vary from time to time and cannot therefore be regarded as specific. It would appear that Wesbrook's types D_2 and E_2 are probably young forms of the more common granular types, and if this be so, caution should be used in reporting a culture negative when only solid forms are found. It is commonly believed that the solid staining bacilli and certain of the barred and granular types are avirulent, but the author's experiments show that this is by no means always the case. He believes, in fact, that morphology as a criterion of virulence of diphtheria bacilli has no more foundation than a similar belief in the case of pneumococcus, for example. From the standpoint of prevention the best criterion is the history of the carrier state. If the history indicates contact with an active case of diphtheria the strain should be considered to be virulent unless proved to the contrary by actual animal experiment. Agglutination tests were made on 206 strains of diphtheria bacilli which included most of Wesbrook's types, a monovalent serum being prepared from a culture showing the constant characters of type C. Of the 206 strains 169 were agglutinated to titre (1:4,860). The 37 strains which failed to agglutinate in any dilution of serum showed no morphological or cultural peculiarities. One of the 37 strains was employed for the production of an agglutinating serum and the latter brought down all the 37 strains to titre. There would thus appear to be two groups differing agglutinogenically, 82 per cent. of the strains examined belonging to one and 18 per cent. to the other. No evidence of cross-agglutination was disclosed, and, in both groups, typical granular diphtheria bacilli of high-grade virulence for guinea-pigs were found, and the proportions of Wesbrook's types were about the same. Experiments in which standard antitoxin was used to neutralize the toxin produced by one or other of the two agglutination groups showed that the differentiation was not so complete, as group antitoxins common in both groups seemed to exist in small amounts, and these results were confirmed by Schick tests. The author considers that his experiments may throw some light on the cases of diphtheria which do not react except to large doses of diphtheria antitoxin, such cases being possibly due to bacilli of Group 2. He thinks that the inclusion of a representative of Group 2 in the production of therapeutic antitoxin would greatly increase its efficiency, and might lower the mortality of diphtheria in proportion to the incidence of strains of the agglutinogenic Group 2.

W. B.

Durand, P. Agglutination des bacilles diphthériques. Préparation des sérums — techniques de l'agglutination et de l'adsorption des agglutinines. [**Agglutination of diphtheria bacilli; the preparation of agglutinating sera and the technique of agglutination and absorption.**] *Compt. rend. Soc. de biol.*, 1920, **83**, 611.

For the preparation of agglutinating sera for diphtheria the author recommends normal or antitoxic horses to which he gives series of three intravenous injections, at 24-hour intervals, of living diphtheria bacilli.

To begin with, the first three injections are of quantities of 1 to 2 mg. of bacilli (weighed moist). After an interval of 7 days following the last injection the dose is increased, the quantity employed being such as to produce a febrile reaction. The maximum doses injected were 250 to 350 mg. After 2 to 3 months' treatment the animals were bled 7 days after the last injection and the agglutinating effect tested. Titres ranging from 1 : 6,400 to 1 : 25,600 were obtained. Goats were also found useful, but rabbits were unsuitable. For antigen the author used cultures grown on coagulated horse serum, the cultures being suspended in 0·8 per cent. salt solution. After standing on ice for 24 hours, during which the main clumps of bacilli settle, the supernatant homogeneous emulsion is employed for the test which should be the macroscopic one. Incubation was carried out at 45°–55° C. and the reading was made at the end of 6 hours. Absorption of agglutinins was carried out by the usual technique. W. B.

Durand, P. Les types de bacilles diphthériques déterminés par les épreuves d'agglutination et d'adsorption des agglutinines. [**Types of diphtheria bacilli determined by agglutination and absorption tests.**] *Compt. rend. Soc. de biol.*, 1920, **83**, 613.

The author tested the agglutination reactions of 255 strains of typical diphtheria and 84 of pseudo-diphtheria bacilli isolated from the throat, nose, conjunctiva, skin, urethra, and cerumen. Eighteen diphtheria strains had to be excluded as it was impossible to obtain a stable emulsion with their cultures. The remainder were divisible into six groups, of which five, named A, B, C, D, and E, were well marked and contained 16, 8, 25, 61, and 40 respectively of the author's strains. He points out that agglutinating sera from rabbits were often less strictly specific than similar sera obtained from horses. A further study of the 87 strains which were inagglutinable by the five type sera showed that nevertheless they could absorb the agglutinins from such sera, the final figures for the five groups of bacilli being 18, 8, 31, 76, and 51 respectively. None of the 60 pseudo-diphtheria strains which could be utilized were agglutinated to any degree by true diphtheria agglutinating sera, and none absorbed diphtheria agglutinins.
W. B.

Brightman, C. L., Meachem, M. R., and Acree, S. F. A spectrophotometric study of the 'salt effects' of phosphates upon the colour of phenolsulfonephthalein salts and some biological applications. *J. Bact.*, 1920, **5**, 169.

The experimenters were led to this work by their investigations on the limiting values of the hydrogen-ion concentration for wood-destroying fungi. It is known that the presence of certain salts have an appreciable effect on the apparent values of the hydrogen-ion concentration obtained by the electrometric and colorimetric methods. In particular the authors have studied the salt effect of phosphates on phenolsulphonephthalein.

Using a tautomeric indicator, K being its apparent ionization constant acting as an acid, α the concentration of the coloured anions, H the hydrogen-ion concentration, and $1-\alpha$ the concentration of the non-ionized molecules, then $K = H\alpha/1-\alpha$. If it is assumed that the colour of the indicator solution is a measure of the amount which has been ionized, then $1-\alpha/\alpha$ can be determined experimentally. If light of intensity I_0 falls on a cell containing a solution of the indicator and the intensity of the transmitted light is I, then $I/I_0 = 10^{-N}$, where N is the absorption index. Let N_a be that index for the middle of the band when the indicator is partly ionized, and N the index for complete ionization. Then $1-\alpha/\alpha = (N-N_a)/N_a$, and if the hydrogen-ion concentration H were known, then $K = HN_a/N-N_a$. The absorption index was measured by a Brace spectrophotometer, and from the readings $N-N_a/N_a$ determined, and thus also $1-\alpha/\alpha$. The hydrogen-ion concentration of each solution was measured by the Loomis-Acree method involving the $N/10$. KCl − HgCl electrode with 4·1 N. KCl as the connecting link. The results of their investigations show that phosphate solutions varying in concentration from $N/2$ downward and showing the same hydrogen-ion concentration (measured by the hydrogen electrode) have marked influence on the colour of phenolsulphonephthalein salts. This 'salt effect' is small in phosphate solutions of low concentration from 0·05 N down. The apparent ionization constant of the phenolic group of the phenolsulphonephthaleins varies with the concentration of the phosphate present and averages about $2{\cdot}65 \times 10^{-8}$ when uncorrected for the 'salt' effect. If corrected by a graphical method it is $1{\cdot}95 \times 10^{-8}$.

A table of P_H corrections to be added to colorimetric P_H for different concentrations of phosphate in order to obtain the electrometric P_H is given.

W. A. M. S.

Legroux, R. et **Menard, J.** Vitamine pour la culture des bactéries. **[Vitamines for bacterial cultures.]** *Compt. rend. Acad. d. sc. Par.*, 1920, **170**, 901.

The extraction of red blood corpuscles with twice the amount of 9 per cent. salt solution at 85° gives a substance which by itself alone is a bad medium for the growth of Pfeiffer's bacillus, but added to peptone meat broth is an excellent medium for this microbe. The active substance passes through parchment paper and collodion sacs and its activity is preserved for a long time (10 months). In addition, red blood corpuscles precipitated with alcohol, dried, and extracted with salt solution at 80° C., show the same properties. Extracts of organs were tried, and only those which contained blood or transformed products of it, such as bile, were favourable for the growth of Pfeiffer's bacillus. An observation of interest is that the more vitamine the medium contains the longer the microbe lives, and it seems that the acidity or other products of metabolism formed in the culture are not the principles which kill or shorten the life of the micro-organisms, but lack of this stimulating substance. A. D.

Jones, H. M. The limiting hydrogen-ion concentration of various types of pneumococci. *J. Infect. Dis.*, 1920, **26**, 435.

In a previous paper (*Jour. Infect. Dis.* 1920, **26**, 160) the author has shown that the limiting hydrogen-ion concentration varies for a given organism, depending on factors which favour or hinder abundant growth.

As the growth of the pneumococcus is greatly influenced by slight changes in environment, the author has sought to establish definite conditions under which the final hydrogen-ion concentrations were developed. When grown in glucose broth, the concentration produced by various types of pneumococci varies between P_H 5·0 and P_H 5·6, being indistinguishable in this respect from various strains of *Streptococcus haemolyticus* of virulent type. The regularity with which these final hydrogen-ion concentration values can be reproduced depends largely on the initial reaction, ordinary glucose broth of P_H 7·0 being useless for this purpose. None of the strains failed to grow when the initial reaction was set at 7·6.

This failure to grow in broth of P_H 7·0 does not account for the often observed failure to secure growth of the pneumococcus, as when blood-cultures are being made, since the addition of 2 per cent. of whole blood renders the medium of P_H 7·0 even superior to glucose broth of P_H 7·6 in stimulating growth. A marked increase in tolerance toward the hydrogen-ion is also observed, as is also the case with *Streptococcus haemolyticus*.

W. A. M. S.

Harvey, W. F. The tinturometer, an instrument for measuring tint and turbidity. *Indian J. M. Research*, 1919, **7**, 346.

Ibid. Measurement of bacterial content in fluid suspension. *Indian J. M. Research*, 1919, **7**, 352.

The tinturometer is an instrument designed to measure the concentration of suspensions, whether tinted or colourless, and also the depth of tint of a solution. The author suggests its use to measure the degree of growth of organisms in fluid media of different compositions, the concentration of erythrocytes in the blood, and the haemoglobin content of blood. The apparatus consists of a graduated cylindrical measuring tube of 10 c.c. capacity, and some instrument to supply a figure whose degree of visibility is to be the measure sought for. The author uses a steel foot-rule, but other arrangements are suggested. The use of the instrument is as follows: Fill the cylinder with the fluid to be tested, and place the foot-rule on a sheet of white paper. Now stand the cylinder over a selected number on the rule and remove fluid from the tube with a pipette till the selected number is just visible. Read off the number of c.c. left in the cylinder and compare with that given by a normal or standard fluid. As a simple turbidity standard he uses a 1 in 8 dilution of 1 per cent. barium sulphate in 1 per cent. sodium citrate solution. Coloured suspensions and solutions can be similarly used.

The second paper contains the results of a series of applications of the use of the tinturometer together with some improvements in the technique employed. Ten different sets of experiments were carried out (on *B. typhosus* or *B. coli*) showing the influence of the following factors on growth:

Various brands of peptone; varying concentrations of Witte's peptone; addition of sugars in different proportions to peptone water; seed culture added to Witte's peptone; duration of incubation period; age of medium; addition of calcium chloride, sodium citrate, trypsin and meat abstracts; and the addition of various substances to a simple synthetic medium.

W. A. M. S.

BIOCHEMISTRY

Gillespie, L. J. Colorimetric determination of hydrogen-ion concentration without buffer mixture, with especial reference to soils. *Soil Science*, 1920, **9**, 115.

This method ought to be of considerable service to those who are investigating the reaction of fluids and who are unable to procure the pure chemicals necessary for making the requisite buffer solution. It will also be of value in the important range of acidity covered by methyl red, the colour of which fades. The only equipment absolutely necessary is a suitable solution of an indicator and a dropping pipette. A somewhat similar method was detailed in 1918 in the *J. Amer. M. Ass.* **70**, 1062, by Barnett and Chapman.

The principle of the method is the partitioning of a definite number of drops of an indicator solution between two tubes. One of the tubes is made acid, the other alkaline. Light passing through the two tubes placed one behind the other traverses a layer containing a certain concentration of an acid solution and a certain concentration of an alkaline solution. The resulting colour is the same as if a buffer had been employed. By variations in the partition of indicator between the acid and alkali tubes any shade may be obtained. A comparison is then made with a tube containing the fluid to be examined, to which the total number of drops of indicator are added. A table, in which a complete range of indicators is given, shows the hydrogen-ion exponent for each drop ratio. Preliminary tests made by the present abstractor seem to indicate that the method is of very real utility. The theory of the method is discussed in detail.

C. G. L. W.

Parsons, T. R. The reaction and carbon dioxide carrying power of the blood. A mathematical treatment. *J. Physiol.*, 1920, **53**, 340.

The changes in hydrogen-ion concentration produced in blood as the result of change in carbon dioxide tension are such as occur in a system consisting of carbonic acid and one other weak acid of constant strength, with a fixed total amount of sodium distributed between them. The second weak acid which forms part of this system in the blood is chiefly, if not entirely, haemoglobin. Blood possesses greater efficiency as a 'buffer' solution than does a bicarbonate solution; it is therefore obvious that sodium bicarbonate cannot be the only buffer substance in the blood. Haemoglobin plays a part in the production of this buffer effect, and the same is probably true of the plasma proteins. H. M.

Coleman, W. M. The influence of the state of the blood on the interworking of the eyes. *J. Physiol.*, 1920, **53**, 361.

An experimental study into (1) the effect of phases of rest and work in regulating the activity of the eyes and (2) the apparent ability of the eye to function continuously.

The conclusion arrived at is that the eyes function equally when respiration is efficient, but that with defective respiration they work alternately and so rest each other. The cause of this is undetermined: it may be due either to lack of oxygen or to the presence in the blood of metabolic products.

Stereoscopic vision requires a higher degree of ventilation of the blood than panoramic vision. With efficient ventilation equality of vision in the two eyes is preserved, the two nasal fields and the two temporal fields functioning more vividly by turn. When ventilation is defective each eye as a whole alternates in vividness with its mate. H. M.

Bazett, H. C. The time relations after excision of the adrenal glands, with some observations on blood volume changes. *J. Physiol.*, 1920, **53**, 320.

On excision of the adrenal glands in cats, blood-pressure changes soon develop; the period after excision at which these changes appear depends to some extent on the anaesthetic used. In the decerebrate animal the changes develop earlier and progress more quickly than in one anaesthetized with urethane. When ether is used, and the animal is allowed to recover from the anaesthetic, the blood changes are not so rapid. With a fall of blood-pressure due to prolonged urethane anaesthesia, little or no dilution of the blood is found. This is in marked contrast to what happens when the blood-pressure falls as the result of haemorrhage. H. M.

Hartman, F. A. and **Blatz, W. E. Studies in the regeneration of denervated mammalian muscle.** *J. Physiol.*, 1920, **53**, 290.

A functional test is fully described by means of which the relative power of the gastrocnemii group of muscles of the two limbs of rabbits may be compared at frequent intervals. Using this test in conjunction with denervation experiments, it was found that neither massage nor galvanic treatment appeared to benefit denervated muscle. Neither form of treatment helped to hinder the loss of response to galvanic stimulation or hastened the recovery of the muscle. When denervation was accomplished by crushing the nerve, the muscles regained both their voluntary force and their power to respond to galvanic stimuli several weeks earlier than was the case in muscles denervated by cutting the nerve. H. M.

Zwaardemaker, H. On physiological radioactivity. *J. Physiol.*, 1920, **53**, 273.

In a large number of systems in the animal organism the potassium ion may be replaced, as far as function is concerned, by all the other radioactive elements. When applied simultaneously, substances emitting α rays and those emitting β rays are reciprocally antagonistic. Potassium has the property of stimulating many cells and can restore and sustain function when it is brought in contact with the surface of the cell as a free diffusible ion in the circulating fluid. In isolated hearts, brought to a standstill by the removal of potassium and perfused with a potassium-free fluid, the pulsations invariably returned when a tube containing a few milligrams of mesothorium was held near the organ. Removal of the mesothorium caused a standstill.

Evidence is adduced to show that a cessation of cardiac pulsation may be brought about not only by a deficiency, but also by an excess, of radioactive substance. H. M.

Gray, J. The relation of the animal cell to electrolytes. *J. Physiol.*, 1920, **53**, 308.

A study of the probable function in development of the electrolytes and globulins of the egg of the trout. The normal fertilization of the trout egg is described.
H. M.

Fleisch, A. Enthält der Arterienpuls eine aktive Komponente? [**Has the arterial pulse an active phase?**] *Arch. f. d. ges. Physiol.*, 1920, **180**, 138.

The question as to whether the arterial wall actively takes part in transporting the blood to the capillaries has been examined by a plethysmograph tracing of the artery and a simultaneous tracing of the blood-pressure. It was shown that neither under normal conditions, in lack of blood, due to haemorrhage, nor under the influence of adrenalin was there any evidence of an active participation of the vessel-wall in carrying the blood.
C. G. L. W.

Gaertner, G. Atmungsversuche bei sehr hohem Druck. [**Respiration under very high pressure.**] *Arch. f. d. ges. Physiol.*, 1920, **180**, 90.

It is well known that the solution of nitrogen in the fats, especially of the nervous tissue, is responsible for the disastrous results of too sudden decompression of divers and tunnellers. G. attempted to ascertain whether the use of hydrogen, in a mixture of oxygen and this gas, was less dangerous than air. The results were inconclusive. It is suggested that, as large quantities of helium are now available, it might be possible to use this gas for deep diving apparatus.
C. G. L. W.

Krogh, M. Patologiske Forandringer i Hvilestofskiftet. [**Pathological changes in the metabolism of the body at rest.**] *Ugesk. f. Læger*, 1920, **82**, 539–50 and 577–82.

Marie Krogh has estimated the quantity of oxygen absorbed by the body at rest, and the figures she has obtained may be used, in her opinion, to good effect in the differential diagnosis of ill-defined cases of Graves's disease and myxoedema. This test is also an objective criterion of the effect of treatment on both these diseases. With reference to earlier investigations into the effect of the glands of internal secretion on the metabolism, she attaches special importance to a paper by Magnus-Levy, who showed that the metabolism is below normal in cretins and the subjects of myxoedema, whereas it is considerably above normal in patients with Graves's disease. He also found that the administration of thyreoidin increased the metabolism when this to begin with is below normal.

Dr. Krogh's investigations were made on bed patients in hospital, and in estimating the exchange of gases on respiration she used a Zuntz mouthpiece and other apparatus of which she gives a description. The data obtained were (1) the amount of expired air, (2) the percentage of O_2 and CO_2 in this air, and (3) the time taken in the collection of each sample. The weight of the patient being ascertained, all the factors necessary for a calculation of the metabolism per unit of time (a minute) and surface (square metre) were available for expressing in figures the rate metabolism.

The patients examined were classed under one of the four following headings: (1) Graves's disease, (2) goitre without other definite signs of Graves's disease, (3) myxoedema, (4) adiposity without myxoedema. In the first class the metabolism was 40 to 80 per cent. above normal. In the second class it was 5 to 25 per cent. above normal. Some of these patients exhibited signs indicative of Graves's disease, but, as their metabolism was normal, this diagnosis was rejected. In two such cases the diagnosis of Graves's disease was rejected in favour of neurasthenia, and in a third case in favour of renal glycosuria. Case No. 23 was particularly instructive as showing the importance attached by Dr. Krogh to the value of her metabolism tests in the diagnosis of Graves's disease. The thyroid gland was considerably enlarged, the pulse was rapid and irregular, and exophthalmos and lassitude were accompanied by a series of nervous symptoms. But the metabolism being absolutely normal, the diagnosis of Graves's was rejected. The X-rays showed considerable displacement of the heart, and a diaphragmatic hernia of the stomach.

In one of her many tables, Dr. Krogh includes patients who, with one exception, were abnormally heavy. To decide by clinical examination whether excessive weight is due to myxoedema or adiposity is often difficult. Some of these patients showed a metabolism only 65 per cent. of normal. In other words, their production of thyreoidin was undoubtedly below normal. In four cases the metabolism was normal, and the diagnosis, therefore, was adiposity. As the table shows, the administration of thyreoidin was more effective in promoting metabolism in cases of myxoedema than in those of adiposity. With regard to the administration of thyreoidin, Dr. Krogh observes that large doses are apt to promote metabolism beyond the desired extent, and to upset the organism's equilibrium in respect of certain factors, as the following cases indicate. Two patients, suffering from myxoedema, had been given such large doses of thyreoidin that early exophthalmos, palpitation of the heart, and lassitude were provoked in the one case, restlessness, insomnia, and palpitation of the heart in the other. Controlling the dosage of thyreoid substance by analyses of the metabolism, Dr. Krogh was able to find the exact quantity of the gland necessary for the maintenance of normal metabolism. C. L.

Walbum, L. E. L'influence de la température sur la concentration en ions hydrogène de quelques solutions étalons. [**The influence of temperature on the hydrogen-ion concentration of certain standard solutions.**] *Compt. rend. Soc. de biol.*, 1920, **83**, 707.

The hydrogen-ion concentration of different standard solutions has usually been measured at normal laboratory temperature (18°–20° C.). The author has employed the standard solutions suggested by Sörensen, and has taken readings at 10°, 18°, 28°, 37°, 46°, 56°, 62°, 70° C. The following results were obtained: No variation in the case of phosphate mixtures, glycerine, hydrochloride and citrate, hydrochloric acid. In the glycine-NaOH, borate-HCl, and boric-NaOH mixtures, the hydrogen-ion concentration increased with the temperature, and thus the P_H value diminished. The contrary is the case with citrate-NaOH mixture. In those cases where P_H diminishes with rise of temperature, the temperature variations are relatively greater in the more alkaline mixtures. The variations between 10° and 70° C. follow a linear law, and hence only the values at 10° and 70° C. are tabulated. W. A. M. S.

Van Egmond, A. A. J. Über die Wirkung einiger Arzneimittel bei partiellem Herzblock nebst Versuchen über Entstehen von Herzblock durch oligodyname Metallwirkung. [**The action of certain drugs on partial heart-block and experiments on the production of heart-block by small amounts of metallic poison.**] *Arch. f. d. ges. Physiol.*, 1920, **180**, 149.

Van Egmond published an important paper on the therapeutics of complete experimental heart-block in 1913, and has followed by an investigation of the effects of certain drugs on the incomplete condition. The preparation used was the isolated rabbit's heart perfused with Locke's solution. The drugs investigated were strophanthin, strychnin, adrenalin, camphor, calcium, barium, and physostigmin. Several methods of producing heart-block were tried, of which, touching the neighbourhood of the His bundle with formalin gave good results. The method finally employed, and which is of great physiological interest, is the following: If the vicinity of the His bundle be touched with a piece of bright brass, the heart immediately comes into a condition of heart-block. If bright copper be employed, the effect is more pronounced, and it is only necessary to touch lightly the right side of the septum with a piece of copper wire to bring the ventricle to rest. Van E. shows that the phenomenon is due to the solution of minimal quantities of the metallic ion and is not concerned with pressure, heat, or electrical phenomena. No other of the metals tried had so pronounced an action, but the phenomenon is distinctly seen with zinc and cadmium.

The positive heart-block may continue for 15 minutes. The method proved itself of real value, for heart-block could be produced at will and the therapeutic agent applied immediately after. A detailed description of the experiments and their results are given. The therapeutic conclusions are the following:

(1) Strophanthin hastens the therapeutic stage of conduction between ventricle and auricle. The stage of irregularity comes on more quickly when the conducting path is damaged. The irregularities at the commencement are due to the fact that the sinus nodes must replace the directive action of the deeper cardio-motor centres. There is a change from ventricular beats that are independent of the auricle and later of atrio-ventricular beats and autonomic ventricle beats which, in consequence of reversed conduction, may induce auricular beats. Finally, complete dissociation takes place. This may be partly due to increased contractile stimuli in the ventricles.

(2) Strychnin increases the conductance between auricle and ventricle in the pretoxic stage, and enlarges the ventricular contraction. In total block it effects a decrease in amplitude of ventricular contraction and its frequency.

(3) Calcium chloride has a favourable effect on the conducting of impulses. Larger amounts provoke partial heart-block. In total block it produces attacks of ventricular tachycardia.

(4) Bariüm chloride decreases conductivity and in small quantities increases the state of block.

(5) Adrenalin has little effect. By increasing the auricular frequency one may obtain partial block.

(6) Caffein disturbs conductivity. The length of a partial block or the establishing of a partial block is not due to its specific action on the path, but to the increased frequency of the auricular contractions induced by the drug.

(7) Camphor in large amounts decreases conductivity. In smaller

concentration there is no effect. Concentrations of 1–35,000,000 produce an increase in contraction.

(8) Physostigmin damages the conduction. The block persists or rises to a higher grade. The conduction may, in some cases, be irretrievably damaged. The experiments with this drug seem to have shown a potency beyond almost anything that so far has been investigated. A concentration of eserin of 1 – 50,000,000,000 had a distinct action in increasing the length of heart-block. C. G. L. W.

WINTERSTEIN, H. Die Narkose. [**Narcosis.**] *Monographien aus dem Gesamtgebiet der Physiologie*, 1919, **2**, Berlin: J. Springer.

This is the second volume published in a series which commenced with Michaelis's useful exposition of hydrogen-ion concentration which was issued in 1914. For those who wish to have an insight into the modern theories of narcosis, in which term are included the anaesthetics and hypnotics, this book can be confidently recommended. The question involved is not one of narcotics alone; for the phenomena are so intimately bound up with other vital problems that a study of these drugs will shed light on many fundamental physiological problems. After a very complete analysis of the theory of narcotics, Winterstein puts forward his own point of view, viz. that the action of narcotics, is principally concerned in the adsorption of the drugs on the cell surface. This leads to changes in the surface layer (decrease in surface tension), so that difficulty is experienced in the ionic exchange between the interior of the cell and the fluid in which it exists. The volume closes with a most complete bibliography of the subject. C. G. L. W.

MYERS, V. C. Chemical changes in the blood in disease. *J. Lab. & Clin. Med.*, 1920, **5**, 343.

A critical discussion of the methods which may be usefully employed for diagnostic purposes. The components of the blood which are considered are: blood volume, haemoglobin, non-protein nitrogen, creatinin, sugar, lipoid constituents, mineral salts, blood gases, hydrogen-ions, acetane substances, and enzymes. These are considered in relation to renal diabetes, diabetes mellitus, gout, nephritis, prostatic obstruction, cholelethiasis, pernicious anaemia, and miscellaneous conditions. C. G. L. W.

FISCHER, M. H. A third model illustrating some phases of kidney excretion. *J. Lab. & Clin. Med.*, 1920, **5**, 352.

An investigation of the filtration of water and solution of salts through sodium stearate cups. Fischer believes that this type of membrane closely simulates the mechanism of kidney filtration.

Pure water passes through the membrane without the expenditure of energy. If the water is associated with a hydrated colloid, filtration does not take place. Salt solutions lead to greater filtration; ammonium and potassium salts are the least effective. Magnesium and calcium salts head the list. These findings are analogous to what is observed in clinical practice. C. G. L. W.

ZONDEK, B. Der Einfluss des Hypophysenextraktes auf die Peristaltik. [**The action of hypophysis extract on peristalsis.**] *Arch. f. d. ges. Physiol.*, 1920, **180**, 68.

Zondek has studied the action of the glandular extract by direct observation of the intestine through a permanent window of celluloid healed into the abdominal wall; the method is that of Katsch and Borchers. By each injection of the drug there is a preliminary 'psychic shock' which lasts two minutes, with complete interruption of peristalsis. The hypophysis extract stimulates peristalsis of the large intestine, but occasionally first causes slight inhibition. It also regulates peristalsis. Injections of the drug are recommended in post-operative intestinal atony. C. G. L. W.

HESS, W. R. (1). Viscosimeter mit Temperaturregulierung. [**Viscosimeter with temperature regulation.**] *Arch. f. d. ges. Physiol.*, 1920, **180**, 61.

Hess has improved his viscosimeter for determining the viscosity of blood and other fluids. It may be obtained from E. F. Büchi, optische Werkstätte, Bern, Switzerland. The price is 80 francs. C. G. L. W.

HESS, W. R. (2). Die graphische Aufzeichnung der Herztöne nach neuer Methode. [**A new method of registering heart sounds.**] *Arch. f. d. ges. Physiol.*, 1920, **180**, 35.

A rubber membrane is prepared which is so thin that it shows interference phenomena. To this is attached a piece of platinum wire 0·005 mm. in diameter. This is constructed into a tambour which, with a suitable receptor, is made to vibrate, the vibration being recorded by light. The analysis of the heart sounds show a segmentation of the tone curve of the first heart sound into fore part, tone part, and after part. In any analysis the three parts ought to be measured separately. Figures are given for normal cases. C. G. L. W.

RADIOLOGY AND ELECTROLOGY

Radiotechnique

BERGONIÉ, J. Plates-formes isolantes de protection pour laboratoires de radiographie et radioscopie. [**Insulating protecting platforms for radiographic and radioscopic laboratories.**] *Arch. d'électric. méd.*, 1920, **28**, 50.

The insulating platform described is made of wood boiled in paraffin wax. It is, essentially, a wooden grille 1 metre long, 50 cm. wide and 4 cm. thick. It is in itself a good insulator but is further improved by being mounted on four truncated conical glass blocks, 3 cm. high. If the X-ray operator stands on such a platform he can touch the leads to the tube with impunity. J. R. C.

MAUCLAIRE. L'ablation des projectiles sous l'écran. [**Removal of projectiles under the screen.**] *Presse méd.*, 1918, No. 40. (*Zentralbl. f. Chir.*, 1919, **46**, 229.)

The author lays stress on the fact that there are three different methods of extracting foreign bodies under the X-rays. The surgeon works either directly with a fluoroscope strapped to his head or with his head beneath a black cloth, or he operates under the direction of a radiologist equipped with the fluoroscope (intermittent irradiation), or he extracts the foreign body under the X-rays directly, and without the aid of the fluoroscope. After the eyes have become sufficiently accustomed to the darkness (10 minutes in a dark room) the extraction can be quickly performed. There is no need to fear burning of the operator's hands by the rays in short extractions, but burns can be avoided by smearing the hands with lead rubber (50 grm. rubber solution, 50 grm. petrol, 100 grm. lead-carbonate) or by suitable sterilized gloves. The third method, recommended by the author since 1913, may be successfully used for difficult cases of extraction, such as from the lung or brain.

[The futility of the precaution suggested against X-ray burns is only too obvious, and the suggestion that short operations should be carried out with naked hands is astounding. W. S. L-B.] S. U. L-B.

Radio-biology

Mazérès, G. Sur le phénomène de Radiothérapie. Lois qualitatives et quantitatives. [**The phenomenon of radiotherapy. Qualitative and quantitative laws.**] *Arch. d'électric. méd.*, 1920, **28**, 40.

A general review is taken of the known laws relating to radiotherapy. Three qualitative laws are given. The first, due to Bergonié and Tribondeau, is concerned with the cellular radio-sensibility, and states that, other things being equal, the radio-sensibility of living cells is greater, the greater the karyokinetic activity, the farther advanced the state of division, and the less definitely fixed the morphology and function of the cell. The second law is the result of work by Lafargue, Tribondeau, and Bordier. The radio-sensibility of the cellular albumin is greater the more recently this albumin has been formed. Pegaud and Nogier have enunciated a third law which states that the radio-sensibility of a cell is a function of the wave-length of the radiation. There are also four quantitative laws. That due to Limmem and Marie states that feeble doses of X-rays exercise a stimulating effect on cellular evolution, and on the functioning of the cell. The second of these laws is attributed to Beclére. All living cells, healthy or malignant, having absorbed a sufficient quantity of X-rays, become the seat of chemical changes, terminating in degeneration and death. Guilleminot has found that the biochemical action of a radiation depends on the absorbability of the radiation by the cellular albumin. To these three laws the author adds a fourth, stating that there is a constant relation between the cellular reactions and the manner of partition of the quantity absorbed, throughout the depth of the tissue.

Bordier and Galinard have investigated the effect of the radiations on colloids, and the former has formulated a theory of the biochemical action of the rays. According to this theory the rays precipitate the albuminous colloids which are electronegative. If the precipitation is feeble the cells can recover; if strong, they live for a time on the unprecipitated albumin and then die. This explains the latent reaction period. Newly formed colloids are the most unstable, and therefore most easily affected.

To the laws already given, a general law of dosage is added. The duration of the séance is proportional to the square of the distance from the focus of the tube to the skin, and to the quantity of radiation which is to be received by the region radiated. A graphical method is given for calculating the dose according to this law, taking into account the filter through which the rays may pass, whatever the units of intensity employed, be they those of Bordier, Sabouraud, or Guilleminot. This calculation can also be performed with the aid of a slide rule analogous to that devised by Pilon for radiography. J. R. C.

Bagg, Halsey J. Pathological changes accompanying injection of an active deposit of radium emanation. *J. Cancer Res.* (*Amer.*), 1920, **5**, 1.

This paper is concerned with the effects of intravenous and subcutaneous injections in the white rat. The method adopted was to collect the active deposit from a large quantity of emanation upon crystals of common salt and then dissolve these to the strength of physiological saline. The usual amount collected was about 150 millicuries in 2 c.c. of solution. Details of the method are given in the paper and appear to be adequate. Twelve animals were given intravenous injections, and of these, five, receiving respectively 11, 20, 28, 30, and 135 millicuries, died with acute symptoms, while seven, which received quantities up to 10·6 millicuries, survived and were killed between the fifth and eleventh week after injection for histological purposes. The ten animals in which subcutaneous injections were made received quantities varying from 3·5 to 20·5 millicuries, and again death followed administration of the larger quantities and survival the administration of small quantities (7·0 millicuries and less). Details are given of the histological findings and it is claimed that pathological changes occurred in liver, lungs, kidneys, adrenals, spleen, bone marrow, brain, and vascular system. The most interesting changes were those found in the liver and resulted from comparatively small doses of radium injected subcutaneously. A fatty degeneration associated with many giant cells and hyperchromatic nuclei was found in the liver for a comparatively long time after the treatment. After large doses congestion and haemorrhages were very general and severe in all organs, and in acute cases the animals died with signs of marked enteritis. In the kidney there was a granular degeneration and erosion of the renal cells. The cells of the bone marrow were largely destroyed and replaced by blood, and the spleen was congested and often showed haemorrhages and destruction of red blood cells. The method of injection appeared to determine to a certain extent the severity of reaction in certain organs. Thus after subcutaneous injections there was comparatively little change in the lungs, but with intravenous doses of about the same strength lung lesions were severe, and consisted of proliferation and desquamation of the epithelial cells of the bronchi, marked oedema, congestion, and haemorrhage. Discussing the fate of the radium after its injection, B. concludes that the results of this investigation tend to show that the liver, gastro-intestinal tract, kidneys, lungs, and spleen receive the greatest amount of radio-activity. The histological study tends to show that cytoplasmic changes occurring in the cell are profound and as severe as changes occurring in the nucleus. A similarity was noted in tissue reaction between radium injected intravenously or subcutaneously and radium applied externally. This is interesting in connexion with the fact that observations on animals are now being carried out upon the effects of the gamma rays from five grammes of radium bromide. The abstractor is not yet in a position to speak as to the results of these experiments, but certain similarities show themselves with those described in the paper under discussion. It is not quite certain, however, that the tissues of the rat are entirely suitable for histological purposes on account of the ease with which cytolysis occurs in that animal. There can be no doubt that active deposit is capable of producing very profound changes in a great variety of organs, but some doubt must still obtain as to the exact nature of those changes. In particular, the occurrence of many giant cells and numerous hyperchromatic nuclei in the liver described by the author as a result of the radium injection does not carry entire conviction.

W. S. L.-B.

Waters, C. A. On the treatment of goitre by radiation. *Am. J. Roentgenol.*, 1919, **6**, 622.

W. described experiments he had carried out on the thyroids of dogs. Two terriers were exposed to X-radiation over the thyroid area and given a somewhat indefinite dose, but 'a great deal more than one could give an individual'. Actually one animal received a total of 25 minutes' exposure in 4 sittings in 27 days: epilation was noticed on the 20th day, very severe dermatitis on the 31st day, and on this day portions of the right and left thyroid lobes were surgically removed for histological examination. The other animal received a total of 24 minutes' exposure in 6 sittings in 42 days: epilation and beginning of sloughing were noticed on the 48th day, and on this day portions of the two lobes were removed for histological purposes. The Coolidge tube technique was uniform and consisted of the following: 5 milliampères, 9-inch spark gap, 4 mm. glass filter, 20 cm. focal distance. The right lobe was the experimental one, the left being protected with heavy lead foil. Details of the fixation method are not given. The left lobes must have received some scattered radiation but they differed little from the normal, the cells being rich in protoplasm, the nuclei large, and mitochondria being present in normal numbers. Colloid was present in moderate amount. On the experimental sides the alveolar epithelium was found to be thin and atrophic; often the protoplasm had almost vanished, and it was vacuolated in many places. The nuclei were shrunken, stained poorly, and contained less chromatin than usual. Very few mitochondria were found, and those present stained poorly. Colloid was moderately increased in amount.

In the second animal the changes were similar, but there seems to have been less difference between the control and experimental sides, and the atrophy and shrinkage of protoplasm and nuclei had not progressed to so striking a degree. This fact W. ascribes to the larger size of the animal, and therefore the greater depth of the gland, and to the smaller dose of irradiation given to this animal. He considers, as the result of these experiments, that it is possible to reduce the functional activity of the thyroid by irradiation, and is inclined to ascribe failures in clinical cases to insufficient exposures. It is obvious that much more work must be done before conclusions can be drawn as to the action of radiations upon the thyroid. In particular attention must be directed to different varieties of animals, and to whether the parathyroid is or is not incorporated with the thyroid gland. Experimental work on myxoedema by Gley and by Edmunds and others have shown the importance of these points.

W. S. L.-B.

Radio-diagnosis

Sahatschief. Über die Röntgenuntersuchung der Lungenspitzen in der anteroposterioren (ventro-dorsalen) Lage. [**X-ray examination of apices of the lungs in the ventro-dorsal position.**] *Fortschr. a. d. Geb. d. Röntgenstrahlen*, 1919, **26**, 2. (*Zentralbl. f. Chir.*, 1919, **46**, 1030.)

The author recommends the following position: The patient drops his shoulders as far as possible, leans rather forward with his head stretched upwards. The central beam must pass through the episternal notch. In this position of the patient the shadows of the clavicle and of the anterior portion of the first rib are projected downward and backward, and the apices of the lungs are clearly visible between the corresponding intercostal spaces, which appear larger on the screen. It should be mentioned that in this position the region to be examined is distant from the screen and the picture obtained appears larger, but less distinct. The fact is not of great importance, as it is not the size of the shadows but their density that is to be compared. The author claims the following advantages for this position of the patient: 'The apices become fully visible in the apparently larger intercostal spaces. Since the rays must penetrate through a more extensive part of the apices and also through a lower part of the dorsal muscles, which, here, are not so thick, the smallest shadows of the apices become more easily visible. As the patient leans farther or not so far forward, so one can obtain a greater or smaller expanse of the dorsal part of the upper lobe.' S. U. L.-B.

Ribadeau-Dumas, Mallet et **de Lauterie.** Examen radiologique des viscères abdominaux après injections d'oxygène dans la cavité péritonéale. [**Radiological examination of the abdominal viscera after injections of oxygen into the peritoneal cavity.**] *Bull. et mém. Soc. méd. d. hôp. de Par.*, 1919, No. 31, 952. (*J. de radiol. et d'électrol.*, 1920, **4**, 39.)

This method, tried on the cadaver, then on animals, by Weber in 1913, on living man by Meyer Betz, and especially by Goetze in Schmiedens's clinic, and by Alexandrini under Professor Ascoli, has been proved to be without danger. The authors used Küss's trocar and the insufflation apparatus used for artificial pneumothorax, which enables one to measure the quantity and pressure of gas injected. They injected from 1½ to 2 litres, which was rapidly absorbed, in 24 to 48 hours. The radioscopic and radiographic images naturally vary with the different positions of the patient, and for each position, with the different incidence of the rays. The utility of the method in diagnosis is considerable. Thus, there were seen the shadow of the falciform ligament, the shadow of the liver separated from that of the diaphragm by a clear sickle-shaped space, and on the upper side of the hepatic shadow, umbilicated prominences in a case of hepatic cancer secondary to a new growth of the stomach. The spleen always stood out very clearly. The gall-bladder was often visible. The two kidneys were most often and most clearly seen with the patient in the ventral position; one could judge their situation, their size, and irregularities of their surface. It was also possible to see in the true pelvis the shadow of the fundus and cornua of the uterus. S. U. L.-B.

Stewart, W. H. and **Stein, A. Roentgen ray study of the abdominal organs following oxygen inflation of the peritoneal cavity.** *Am. J. Roentgenol.*, 1919, **6**, 533.

After reviewing the history of this method of technique, the authors go on to give their results in 37 cases. They found that the diaphragm could be completely separated from the liver, the detail of which was better than had even seemed possible. In addition, they could accurately outline the spleen with its pedicle, both kidneys, and, with special technique, the uterine appendages. In one case, a chain of enlarged mesenteric glands was detected. Intraperitoneal adhesions, especially involving the anterior abdominal wall, were easily shown. This method thus opens up a new field for investigation, particularly of the parenchymatous abdominal organs.

The technique is simple; oxygen is allowed to flow gently through an ordinary lumbar puncture needle into the peritoneal cavity until the anterior abdominal wall becomes dome-shaped, usually about 4 litres being required. The patient should be allowed to become accustomed to this distension for about one hour and then the X-ray examination is made. If a longer interval is allowed, emphysema is liable to occur through the peritoneal opening into the outlying structures. The oxygen injected into the peritoneal cavity is gradually absorbed by the abdominal tissues, disappearing almost completely in from 24 to 48 hours.

The cardinal point to be borne in mind when making the X-ray examination is that the particular organ which is being investigated must be placed in the highest plane possible in order that it may be completely surrounded by the gas, and that the intestines, which are freely movable in the presence of oxygen, be allowed to drop away. The authors describe some of the positions which they found most useful.

The factors to be considered in this technique are the danger of infection and the risk of puncturing the intestines. The first can be overcome by ordinary precautions, while the authors say that with care there is absolutely no danger of puncturing the bowel.

In contrast to the opaque meal method which concerns the hollow organs, oxygen inflation of the peritoneal cavity gives information more particularly of the solid structures of the abdominal cavity. In conjunction, it is said, the results should be ideal.

The article is illustrated by some striking skiagrams. R. W. A. S.

Alessandrini, Paolo. Il quadro radiologico della tubercolosi pulmonare. [**The radiological picture of pulmonary tuberculosis.**] *Radiol. med.*, 1920, **7**, 46-75.)

An exhaustive examination of phthisis from the radiological point of view. The opinions are based on X-ray examination, controlled by reference to post-mortem observations whenever possible. For technique the author advises fairly soft rays, 4 to 5 Walter, and intensifying screens. Negatives with good contrast and definition are thus obtained. The most generally useful position is the dorso-ventral, centred on the 4th or 5th dorsal spine, giving a small heart shadow and large intercostal spaces. Stereography is important for demonstration purposes, but its cost and complication are not justified by results in diagnosis. Experimental and other evidence is given for the belief that the hilus shadow in the normal lung is due to blood-vessels and lymphatic glands. The latter give no precise shadow, but contribute to the general effect. The author does not believe in the visibility or existence of hyperplasia of hilus glands in relation to early tuberculosis. Having described the definite anatomical distribution of the lymphatics of the lung he proceeds to a consideration of the pathological chest. A well-defined gland shadow is not necessarily tuberculous, but a circumscribed shadow of the same density as rib almost certainly represents a calcified tubercular gland. Caseous glands give shadows nearly as dense, but with less clear outlines. Pleuritic changes are constant features, being most marked in superficial infections, to the foci of which they act as guides. The hilus glands are most affected on the side of the infection, and the lesions here are extensive, as the glands form a breeding-ground for the bacilli. In children there is further extension by contiguity and by blood paths. Gland involvement is progressively less from the second to the twentieth year, and this gives a clue to the age of onset of the disease. The author summarizes Opie's work by describing two types of tuberculosis of the lung—the focal, which is a constant residue of infantile conditions, and the apical type, which appears from about the eleventh year onwards. The former tends to miliary diffusion, with either rapid spread or rapid cure, and secondary involvement of glands. Apical tuberculosis is of a chronic nature, and does not leave much gland infection.

It is not generally possible to see the primary focus, but the visible gland change at the hilus is in relation with it, proves its existence, and is a guide to its position. The most usual radiological evidences of phthisis are calcification, pleural adhesion, and limitation of diaphragmatic movement. Effusion is less often observed. In the apical type there may be a visible connexion between the focus and the gland; there is none in the focal type. It is important to note that the pulmonary pattern is best defined on the side of the affected gland. This is an expression of disturbance in the corresponding venous and lymphatic territory. In the main the author's observations support the theory of a relative immunity conferred by an infantile focal infection, but the remains of this form can be seen in cases of grave exudative disease of the later type, and show a definite relationship between the infections.

The next subject, discussed at great length, is the possible radiological evidence of the activity of lesions. The tendency of the disease is to diminish normal radiological transparency, but, owing to various complicating factors, there is only diagnostic value in the appearance of small dissociated shadows.

With regard to peribronchitis the author identifies three types of thickening of the lung tissue: (1) The *moniliform*, the striations having the appearance of a string of beads. (2) The *varicose*, with an appearance vaguely characteristic of varicose veins in the legs. (3) The *granulose*. The first has been found in syphilis, and without tuberculosis, so is not typical. The second is typical of tuberculosis. The third is the most definite evidence of active disease. In simpler forms it is of granular appearance; with more advanced disease the striae at different levels can be seen to cross each other, producing a reticular appearance. These cases are described as miliariform, and suggest a possible haematogenous form of disease.

The appearances and types of cavities are carefully described, and their differential diagnosis from bronchiectasis and from the less well-known circumscribed pneumothorax, which may be a cause of confusion.

The presence of sclerosis and calcification suggests, but is not complete proof of, cure, while exudative signs certainly mean activity of disease whatever the clinical picture may be.

The author has seen no evidence that persons whose work entails the inhalation of dust, and consequent development of pneumoconiosis, are more liable than others to tuberculosis.

The heart shadows were carefully investigated in about 500 cases, of whom 300 had severe phthisis. Of these latter 25 per cent. had small hearts, 21 per cent. showed large cardiac shadows; these were advanced cases and the size of the heart was probably due to dilatation rather than hypertrophy.

On the difficult question of the source of infection and the method of spreading, there is a long and reasoned argument. The author favours the view that infantile focal tuberculosis confers such immunity that a later infection, from within or without, follows a modified course. This late infection is usually a breaking down of a remnant of the infantile process, and reaches the apex by means of the lymphatics. There is probability of a less common blood-stream spread in miliary tuberculosis, and the air-passages may carry infection in an acute case, but very rarely.

N. H. M. B.

Electro-diagnosis

Perthes. Beobachtungen bei electrischer Reizung freigelegter verletzter Nerven im Vergleich mit dem neurologischen und histologischen Befunde. [**Observations on electrical stimulation of exposed injured nerves compared with the neurological and histological states.** *Deutsche med. Wchnschr.*, 1919, No. **33** (*Zentralbl. f. Chir.*, 1919, **46**, 989).

The author's paper bears upon 432 cases of nerve injury, in some of which several nerves had been subjected to operation. Stimulation of the exposed nerves often produced convulsive movements where electrical examination before the operation had shown defective reaction or reaction of degeneration. Sometimes with complete solution of nerve continuity muscles contracted which normally had nothing to do with the injured nerves, and this, when there was no possibility of current overflow; fibres of the severed nerves must have grown into the neighbouring muscles. He found reaction, however, from direct stimulation in cases of complete exclusion where as much as 3 cm. of scar-tissue lay between the ends and where motor and sensory impairment obtained. Occasionally the contraction could only be induced from the peripheral end. The author's attention was drawn to these conditions from his observations when dividing completely useless nerves for purposes of resection and suture. More or less sharp contractions often occur at the moment of cutting in the region supplied by these nerves. In resected scar-tissue which involved the ends of nerves that had been completely divided Schultz (Würzburg) invariably found besides medullated nerve-fibres, young regenerated fibrils arranged in a confused twisted mass. This observation corresponds with the fact that excitability after complete division of nerves by gunshot wound was never found in cases which were operated upon earlier than 10 weeks after the injury occurred. In the cases upon which the author operated the period between lesion and operation varied from 2½ to 32 months. He explains these phenomena by assuming that young, developing nerve-fibres require a relatively powerful stimulus for their excitation. From the fact that the excitability of the peripheral end is sometimes greater than that of the central end, one must conclude that the peripheral end of the nerve also takes an active part in the regeneration. An excitability that obtained at first was often lost after simple freeing of the nerve; a proof that that excitability rested on newly-formed fibres which had surrounded the cicatricial part and had served to conduct the impulse. Therefore from these results one must recognize the fact that anatomical re-establishment of continuity by means of medullated fibres does not guarantee functional continuity. If one cannot expect spontaneous recovery after the time which has elapsed since the injury (as a rule, a matter of years) the scar must be resected, even though one be convinced that in it the medullated fibres have brought about anatomical union between the two ends; a large and dense scar does not appear to permit of functional re-establishment such as a thin scar would allow. If one finds, however, months after the injury, that there is little change in the nerve when it is exposed and that it is susceptible of direct stimulation, one must conclude that the fibres are not yet sufficiently advanced in development to allow of normal transmission. Treatment must then become very conservative and confined, in case of necessity, to an operation for freeing the nerve, as the author did with success. S. U. L.-B.

Radiotherapy

GRACE, J. J. X-ray treatment of scar tissue due to wounds. *Am. J. Electrotherap. & Radiol.*, 1919, **38**, 298.

Dr. Grace compares the slow progress made with chlorine ionization with the much more rapid improvement following X-ray therapy for localized fibrosis. Scars adherent to bone do not show such satisfactory results as others. If improvement is going to take place, especially in cases of fibrosis round a nerve, it begins to appear after three or four exposures. The results in painful stumps are irregular, often because of retained foreign bodies such as cloth, which cannot be expected to be absorbed as the result of X-ray stimulation. Special cases that do extremely well are chronic mastitis, old-standing facial paralysis, and painful subcutaneous thickenings after tenotomies. It is most probably by its selective action on poorly organized tissues that the X-ray produces its good results.

The conditions treated being chronic ones, there is no hurry to produce results, and the rule for treatment should be 'safety first'. Hence the following technique has been used:

Hard tube with 6 in. equivalent spark gap, 1 ma. in the tube, 12 in. distance, 10 minutes' exposure on alternate days. 1 mm. filter for superficial cases, 2 mm. for deeper ones. N. H. M. B.

MACKEE, G. M. Les rayons X et le radium dans le traitement de l'épithélioma basocellulaire. [**X-rays and radium in the treatment of rodent cancer.**] *J. Cutan. Dis. incl. Syph.*, 1919, **38**, 179. (*Arch. d'électric. méd.*, 1919, **27**, 346.)

In 1899 Steenberk (Stockholm) and Sjögren presented the first cases of rodent cancer treated by X-rays. From 1910 to 1916 the author treated personally 258 similar cases. But 36 did not reappear after the first application, therefore the statistics refer to 222 cases only. Of this number, in over 80 per cent. clinical cure was effected; in some 15 per cent. there was noticeable improvement, and in 2 per cent. the lesions were not modified by the treatment. Taking into consideration the fact that these cases had not been specially chosen, and that a good half of the incomplete results were due to the fact that the patients did not attend on the days fixed for the second or third irradiation, the very high proportion of clinical cures should be regarded as quite satisfactory. The lesions treated had existed over periods varying from some months to several years, and varied in superficial area from a few millimetres to several sq. cm. Ten Benoist rays seemed to give the best results in treatment. The dose employed in each irradiation was 2 H, and was repeated from one to six times according to the type of case. But no specification is given as to filtration. Radiotherapy, preceded by scraping or by excision, appeared to constitute the best treatment for these growths. As to applications of radium, one may affirm that in those cases which are not amenable to the X-rays, radium effects cure, but X-rays cannot cure cases which have proved resistant to radium applications. Finally, in cases of superficial epithelioma of small size the author considers beta rays to be far superior to X-rays, but that no difference seems to exist between the effects of the latter and of gamma rays. Presumably throughout the paper reference is made to rodent cancer alone: though the word 'epithelioma' is used, squamous cell carcinoma can hardly be implied in view of the high percentage of successes claimed. S. U. L.-B.

Eisen, P. Technique of radiotherapy. *Am. J. Roentgenol.*, 1919, **6**, 559.

Eisen says that with the removal of the skin the appearance of the cancer bed and surrounding tissue furnishes the signs for measuring the dose. This dose he has found to be many times that tolerated by the skin. Ten, twenty, and even more full erythema doses in as many successive days have been given. A superficial green-coloured necrosis, less than an eighth of an inch thick, follows this rapid-fire treatment. In a few days the dirty-looking connective tissue returns to its original pink, in which the scattered islands of persistent cancer still remain discoloured. Later, this deeper necrosis sloughs away, the easily-bleeding cancer islands reappear, and the treatment is then renewed.

The only filter against the soft rays used is a four thickness piece of gauze placed over the wound, and a sheet of writing-paper placed over this. R. W. A. S.

Beck, E. G. The open method of surgery in deep-seated recurrent cancer preparatory to Roentgen and radium therapy. *Am. J. Roentgenol.*, 1919, **6**, 559.

Beck considers that one of the most essential requisites for efficient radiotherapy in recurrent cancer cases is the proper preparation of the cancer field, and this he thinks has been overlooked by surgeons. The new method he advocates for these apparently hopeless cases of recurrent deep-seated carcinoma is a transformation of the deep-seated cancer field into a superficial one. To do this he removes all the tissues, skin, fat, muscle, and as much of the tumour as feasible, leaving the cancer bed widely exposed, so that the rays penetrate directly into the seat of the malignant growth.

After the growth has apparently disappeared, the skin from the edges of the wound gradually creeps in and covers the entire surface with the aid of the adhesive-plaster method. This growth of skin he considers proof that the cancerous growth has been eliminated, because healthy epithelial cells will not grow over cancer tissue.

From some experiments by the photographic methods, he finds that the skin absorbs as much as three-fifths of a millimetre in thickness of aluminium, which is considered by radiologists a substantial filter for the rays. Half an inch of fat arrested, on the average, as much as two-fifths of a millimetre of aluminium, while three-quarters of an inch of muscle absorbed three times as much as one millimetre of aluminium.

From these experiments he concludes that in order to have the full measure of the effective X-rays reaching the tumour, the skin, the fat and muscle, and as much of the tumour as possible must be removed.

R. W. A. S.

Radium Therapy.

Condamin and **Nogier.** La radiumthérapie en gynécologie. [**Radium-therapy in gynaecology.**] *Lyon méd.*, 1919, **8**, 372. (*Arch. d'électric. méd.*, 1919, **27**, 346.)

In continuation of their study on radium therapy in gynaecology, of which the first conclusions have been analysed,[1] the authors, when drawing clinical conclusions based on 750 observations, give the indications of this form of treatment in uterine cancer. The results obtained therefrom are more than encouraging; nevertheless, at the present time, hysterectomy is still the best form of treatment, provided that the patient be given the benefit of an irradiation which comes to the aid of surgical removal. After eliminating (*a*) cases justifying from the first surgical intervention, and (*b*) cases inoperable and particularly incurable because of their extent, shape, and metastases, the authors form four categories: (1) 'Uterine cancers developed to the point termed "border-line" which will subsequently have to be operated upon.' In these cases pre-operative radium therapy improves the prognosis, making intervention easier, by lessening the dangers of infection, by diminishing secretion, and by improving the general state of the patient. (2) 'Uterine cancers clearly inoperable at first, in which hysterectomy becomes justifiable after the application of radium.' In these cases, after the radium treatment, surgical intervention is no longer 'operative juggling'. (3) 'Extensive uterine cancers only temporarily improved by the application of radium.' In these unfortunate cases, formerly simply justifying morphin, a large dose of radium can, for some time, give to the patient an illusion of cure by prolonging existence and lessening pain. (4) 'Post-operative recurrences.' It is evident that in deep recurrence, accompanied or not by metastases, the effect of radium is nil; it is not so in the other cases.

These four categories involve an absolute indication for radium. There are also two others where the application of radium, without being as imperative, is strongly indicated: (1) 'Certain operable uterine cancers, especially infiltrating forms in young women where the results of operation are deplorable.' (2) 'After hysterectomy with insufficient removal in order further to deal with a neoplasic propagation.' The authors conclude that, at present, large doses of radium, 150 to 250 milligrammes for 48 hours, should be applied in order to obtain lasting effects after one application, and wait for the future to decide whether knife or radium give the best results.

S. U. L-B.

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[1] *Arch. d'électric méd.*, 1918, 26, 189.

MEDICAL SCIENCE

ABSTRACTS & REVIEWS

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NOTICE

Owing to increases in wages and in the price of paper, the cost of production of 'Medical Science' has risen by 50 per cent. since October, 1919. The Medical Research Council are therefore compelled to raise the price per number to Three Shillings and the Annual Subscription to Thirty Shillings.

REVIEWS

PNEUMONIA

Epidemiology. Zander describes an extensive outbreak of severe pneumonia due to Friedländer's bacillus, which occurred in a prison camp between December 1916 and April 1917. There were 411 cases with 144 deaths, a mortality of 36 per cent. of the 399 cases in the camp hospital. The average number of admissions per day was 3·7. The highest numbers admitted on a single day were: 13 on December 16, 1916; 14 on January 29, 1917; 10 on January 30, and 12 cases on January 31. On January 27, 0·79 per cent. of all those in the camp had the disease. On the coldest days the admissions were highest and the shortage of coal seemed to be partly responsible for this high incidence. Admissions were higher during the prevalence of a west or north-west wind than at other times. The average age of all those in the camp was 29 years, whilst that of the patients suffering from pneumonia was 25½. The incidence of disease was highest for those in their nineteenth year, viz. 41, but the highest mortality was found in those from 39 to 47 years of age, amongst whom there were 21 deaths out of 41 cases (51·2 per cent.). The rate of mortality for those between 17 and 27 years was 60 deaths amongst 246 patients. There were practically no cases in other camps near by and in the neighbouring town of 'X'. Here almost the same conditions prevailed, so that the disease may be regarded as a true 'endemic'.

Bacteriology. Spooner has collected the results of bacteriological examinations in 2,980 cases of lobar pneumonia, 1,103 of which were observed by him at a Base Hospital in the U.S.A., whilst the remaining ones were from various sources. Twenty-nine per cent. of the cases were caused by Type I pneumococcus, 21 per cent. by Type II, 11 per cent. by Type III, and 39 per cent. by Type IV.

Park and Chickering report that at Camp Jackson, South Carolina, between December 15, 1915, and February 1, 1918, *Type I pneumococcus pneumonia* was much more frequent amongst a body of Porto Rican labourers than amongst the white and black troops in the same hospital. The Porto Ricans showed 34 instances of Type I infection in 52 cases of pneumonia; there were 1 in 106 cases of pneumonia amongst the white soldiers, and 2 in 21 cases of pneumonia amongst the black. It would seem that the Porto Rican labourers were more susceptible to infections with this type than with the other three. They were of very poor physique, many suffered from chronic hookworm infection as well as from affections caused by other intestinal parasites, and they slept in very crowded huts where there was abundant chance for the spread of pneumonia. Thirty-one of 33 cases were treated with Type I anti-pneumococcus serum and only two died. Serum sickness showed itself in only 4 of the 31 treated cases, whilst among whites it occurs as a rule in about 80 per cent. of cases treated.

Hirshfeld, Loewe, and Wallach describe a new *method of typing pneumococci,* which is based upon the observations of Rosenow, and also of Longcope, that a coagulum is produced if pneumococci are grown in the blood of a pneumonia patient. This clotting is thought to be due to the production of acids, probably from the glycoproteins of the blood serum. This ability to form a clot is found by Hirshfeld, Loewe, and Wallach to be specific for the different types of pneumococci. Briefly, the method consists in laking a small quantity of blood of the patient with ether, removing the red cells, and adding the fluid to tubes containing saline emulsions of Types I, II, and III; a fourth tube being used as control. The emulsions must be made from actively growing cultures and sterile precautions must be observed. The tubes are kept in a water bath at 37° C. until the colour-change appears. The chemistry of the reaction is not known exactly, but haemoglobin derivatives first appear, giving a brownish-red colour; finally a dark, brownish-red, gelatinous clot is formed. The average time which elapsed before the colour-change occurred was from 6 to 8 hours; the shortest time was 2 hours. Possibly by spectroscopic examination of the blood a specific reaction may be detected after a still shorter interval. Tests were done on 52 cases and in 49 the results were confirmed by agglutination with organisms isolated from the sputum or after puncture of the lung. In the three remaining cases no sputum could be obtained as it was 12 to 14 days after the crisis. This coagulation test was found to be positive as early as the second day of disease. No opportunity was offered of taking blood on the first day. In three cases the reaction was absent after the crisis. Two advantages are claimed for this method of typing the pneumococcus; blood may always be obtained, whilst sometimes there is no sputum, and it is claimed that mixed infections with different types may be determined. Unfortunately one must admit that the method has not been given a very extensive trial.

Symptomatology. Zander describes some of the clinical aspects of a severe form of endemic *pneumonia* (411 cases) *due to Friedländer's bacillus.* In sharp contrast with the acute onset of the pneumococcal form, there was usually a prodromal stage of one or two days, marked by general malaise. Only one-third of the cases began with a sudden chill. In by far the majority of cases the disease first attacked the lower lobes; the right 188, and the left 147 times. In 18 cases the right middle lobe was first attacked, in 10 cases the right upper, and in 3 cases the left upper lobe. In very many instances, on first examination, a number of lobes were found affected. On an average, fever persisted for 9·5 days; the extremes being 2 and 48 days. Recovery by crisis occurred in 131, and by lysis in 127 cases. At the beginning of the epidemic the cases were like true croupous pneumonia, but later on the cases took on more of a broncho-pneumonic character. It is of interest to note that after the patients were convalescent, their sputum, even for a long time, still contained Friedländer's capsulated bacillus.

It is well known that *central pneumonia* may be exceedingly difficult to diagnose, and Sofrè thinks that this form of the disease does not receive from writers the attention it deserves. The general impression has been that physical signs are absent, but Sofrè disputes this. It is true that dullness and blowing breathing may not be found either early or even late in the disease. If these signs appear about the fifth day the author terms the disease 'centrifugal pneumonia' in contrast with true 'central pneumonia', where the inflammatory process never reaches the surface of the lobe. In this later type, only a very small central portion of the lung may be affected, and, as is naturally to be expected, physical signs and 'functional' signs are fewer than in the 'centrifugal' variety. Even dyspnoea, rusty sputum, and pain in the side may not be present, but it is not true that the cough is lacking. This latter may be very slight and almost pass unnoticed by the patient himself. The physician must question him carefully on this point. In cases where there is merely high fever, with no signs of consolidation of the lungs, very slight cough becoming a little more frequent with later a little yellowish-red expectoration, and with the additional phenomenon of a crisis in the temperature curve about the seventh to ninth day, then there is no doubt as to the diagnosis. Sofrè has investigated these cases more closely and has recorded two findings of great aid in diagnosis; (1) over one lobe—perhaps over the whole extent of it—there is a hyperresonant note as compared with that of the opposite side; (2) the breath sounds are relatively feeble. These signs may remain practically unchanged until several days after the temperature has dropped. However, as the cough becomes more productive, the hyperresonance gradually diminishes and the breath sounds are better and better heard. The author explains these signs by assuming that there is a 'peripheral emphysema' about the centrally placed consolidated lung.

Robitschek discusses the difficulties in explaining the vagaries and apparent inconsistencies in the physical signs of *lobar pneumonia* and especially in those cases which simulate *pleurisy with effusion.* There is dullness, but breath sounds are absent, voice sounds are decreased, and tactile fremitus is impaired. The explanation may be that the bronchi are blocked with fluid or mucus, or there may be a massive pneumonia (Grancher) where the bronchi are involved in the general inflammation and are filled with fibrinous exudate. Other cases, however, have been seen at autopsy in which neither of these explanations was possible; nor would Weintraud's idea hold, that the bronchi were compressed by the swollen bronchial lymph nodes. Robitschek suggests that in certain patients with a rigid or 'paralysed' thorax, when the lung becomes enlarged and extensively hepatized, the thoracic wall does not give and the ribs make deep impressions on the surface of the organ, and at the same time, by the increased pressure in the pleural cavity, the bronchi may be flattened out. Thus breath and voice sounds are poorly transmitted. Robitschek admits that at autopsy, after the thorax has been opened up, it is impossible to prove his point. Further, with such a rigid thorax, a moderately-sized interlobar empyema might compress the lower lobe so that rib impressions would be caused and the bronchi compressed, giving the physical signs of an effusion into the general pleural cavity.

Lissner makes a plea for the advantages of employing the *whispered voice* in defining areas of consolidation. In influenzal pneumonia it was extremely difficult to diagnose patches of consolidation, and this was impossible if percussion were relied upon. And if the patient were urged to breathe deeply to bring out bronchial breathing, an exhausting attack of coughing often resulted.

Complications. Amongst 411 cases of Friedländer bacillus pneumonia Zander records 20 with empyema. In 13 out of the total number of cases there was a relapse of the pneumonia with 3 deaths. Tuberculosis followed a few of the cases of pneumonia. Transitory oedema of the legs without albuminuria was recorded in 9 cases. Twice abscesses occurred in the pectoral muscles, but, in spite of the virulence of the causative organism, only one case was seen with multiple abcesses in the subcutaneous tissues and internal organs.

Stone describes 72 instances of *pericarditis* in 300 post-mortems on pneumonia cases in a Base Hospital at Fort Riley, Kansas. There were, in addition, 12 examples of hydropericardium. Fourteen of the cases of pericarditis were of the sero-fibrinous variety. This was found in 11 cases of lobar and 3 times in pneumonia of the bilateral bronchial type. The amount of fluid varied from 250 to 1,000 c.c. Acute purulent pericarditis occurred in 44 cases; in 30 of lobar pneumonia, in 11 of broncho-pneumonia, and in three of the cases both kinds of pneumonia were present. The amount of fluid varied from 100 to 1,000 c.c. Subacute fibrinoplastic and purulent pericarditis ('shaggy heart') was observed 14 times with lobar pneumonia, and with broncho-pneumonia in 6 cases. In about 75 per cent. of the cases the pericarditis was caused by the streptococcus, usually of the haemolytic variety. The organism generally corresponded with that isolated from the pleural fluid. In 33 of the cases there was bilateral pneumonia, in 18 pneumonia of the right lung, and in 21 cases pneumonia of the left lung only. It has usually been thought that pericarditis is more frequently associated with pneumonia of the left lung. The most important factor in the development of the pericarditis was empyema, as 63 out of the 72 cases had this complication as well. Any one of the three forms of pericarditis was likely to occur with empyema. Acute purulent pericarditis was especially apt to be found with an empyema of the left side.

The most important sign in the diagnosis of pericarditis was a to-and-fro friction which sometimes could be felt, and occasionally this was best heard below the angle of the left scapula, being transmitted through consolidated lung, although generally best made out at the base of the heart. The X-ray was most useful in diagnosing the effusion. A positive venous pulsation in the neck was sometimes present if the pericardial sac were greatly distended. Dyspnoea was of no great help towards diagnosis, owing to co-existent and extensive trouble in the lungs. Pericarditis was suspected in those patients who continued to have a rapid pulse and a septic type of temperature after aspiration or operation for empyema. Pericarditis was evidently caused by direct extension if empyema were present. It is to be regretted that Stone does not state the number of cases of pericarditis diagnosed before death, and that no mention is made of an associated purulent mediastinitis if it occurred.

Owing to the fact that the majority of the patients had at the same time extensive disease of the lungs and empyema, paracentesis alone was considered as a form of treatment of either of the serous or purulent pericardial effusions. Like nephritis, pericarditis sometimes developed after the empyema and as such contributed largely as a cause of death in empyema, even after efficient pleural drainage had been established. In Stone's opinion, the condition of the patient never warranted incision and drainage of the pericardial sac. In tapping the pericardium the needle was inserted outside the nipple-line in the fourth interspace and pointed inwards and backwards towards the spine. Or again, it was inserted beneath the costal margin in the narrow angle formed by this and the xiphoid cartilage; but often, with empyema present, the diaphragm was higher on the affected side than normal, and this point was unavailable. The needle should be kept close behind the costal margin and pointed towards the left nipple. The ice-bag and morphin were employed to control pain, and, if general sepsis were due to a streptococcus, an intravenous injection of 50 to 100 c.c. of antistreptococcus serum was given daily.

In the subsequent discussion of Stone's paper, one of the speakers said there was less danger than was generally thought in puncturing the heart-wall, as he had often done this without causing harm. He also stated that a small but rapidly increasing effusion, where the sac has no time to stretch, may quickly kill the patient, whilst a more slowly-forming effusion may be well borne. Another speaker had found pallor of the lips, probably due to distension of the sac with fluid, an indication for tapping the pericardium immediately.

Roussel and de Lavergne discuss the significance of five examples of *jaundice* which occurred between January 25 and March 15, 1919, during the third wave of the epidemic of influenza. Two of the patients showed signs of lobar pneumonia of the left lower lobe and the others broncho-pneumonia confined to one lung or of bilateral distribution. Blood culture was positive for the pneumococcus in all cases. Jaundice appeared on the 4th to 10th day of disease; this quickly became marked and bile pigments were found in the urine of all. Only some showed clay-coloured stools. There was enlargement of the liver with tenderness on palpation. Nephritis declared itself with decrease in the amount of urine, which contained albumin, and amounted in one case to 14·5 grm. per litre. The amount of urea in the blood was not determined. One patient showed signs of meningitis three days after the appearance of the jaundice; the cerebrospinal fluid was purulent and contained many pneumococci. Four of the patients died and the fifth received 100 c.c. of antipneumococcus serum daily. The writers point out that, on the whole, jaundice has been rare in the last pandemic of influenza and was not seen as often as in lobar pneumonia.

Roussel and de Lavergne regard these five cases as examples of a hepato-nephritis secondary to a pneumococcal infection and consider that they are not of the primary acute variety (Merklen, Lioust, Bruhl, Pagniez) nor that found in spirochaetosis ictero-haemorrhagica (Garnier, Reilly, Costa, Troisier, Ameuille). Roussel and de Lavergne believe that the biliary retention was due to a lesion of the liver cells caused by the pneumococcus (see work of Lemierre and Brûlé). In two cases it was shown very clearly that it was a 'dissociated retention of bile' and not retention of the bile as a whole, as there were no bile salts in the urine, no itching of the skin, no slowing of the pulse, and, in the one case examined, no evidence of bile salts in the blood serum. The bacteriolytic action of bile and its inhibitory action on the growth of the pneumococcus are well known. The writers prefer to explain the positive blood cultures in their five cases by the fact that there was no retention of bile salts, rather than by the supposition that the pneumococcus was protected by the albumin of the blood or of the tissues, or by the assumption that in the blood the bile is too diluted to cause bacteriolysis or inhibit the growth of the organism. They regard their five cases as additional evidence in support of Brûlé's theory of 'dissociated retention of bile'. Owing to the lesion of the liver cells their activities are more or less suspended; hence bile pigments, 'preformed in the blood', accumulate, and the bile salts, which have their origin in the cells of the liver, are alone absent. Brûlé's recently written book discusses jaundice from this point of view.

Flandin, Debray, and Françon state that a blood-infection with the pneumococcus, with or without localizing signs in the lungs, may be accompanied by signs and *symptoms of acute peritonitis*. These cases may recover without operation. On the other hand, the septicaemia may become more severe and the patient die rapidly and show at the autopsy only a very congested peritoneum with only a few c.c. of turbid exudate and a very distended intestine. In the third and most common form, suppuration takes place and diffuse general peritonitis results, which rapidly causes death if no operation is undertaken.

Prym records a case of *spontaneous pneumothorax* and sudden death on the 10th day of disease in a man of 53 suffering from lobar pneumonia. Just before this occurred the patient felt fairly comfortable. At the autopsy, four hours later, the diaphragm on the right side was ballooned downwards and the pleura contained air and about 50 c.c. of slightly turbid fluid. The upper lobe was crepitant and showed no pneumonia and the lower lobe was atelectatic. The lower part of the right middle lobe was the seat of consolidation, but the upper part, at its upper sharp edge, was air-containing. There was evidently compensatory emphysema here, for the alveoli were distended. With the slightest pressure on the lobe in this part, frothy fluid could be squeezed out (although no cut had been made) through the pleura, but to the naked eye no break in the pleura was perceptible. There was no pneumonia on the left side and no signs of tuberculosis anywhere. The author cannot find a similar case in the literature of spontaneous pneumothorax in an uncomplicated lobar pneumonia. Cases have been reported of rupture of distended alveoli in those suffering from emphysema or in those with 'vicarious' emphysema in tuberculosis of the lungs. Spontaneous pneumothorax has also been found in those who were said not to have had tuberculosis: in healthy men when lifting heavy weights, when laughing unusually hard, or even in cases where no extraordinary effort was put forth. In these patients, however, latent tuberculosis was not rigidly excluded by post-mortem examination. Prym concludes that in his case there must have been rupture of a distended air sac although the perforation in the pleura could not be definitely found. He closes his article with the conjecture 'perhaps under abnormal conditions the pleura, although uninjured, may be permeable to air'.

Treatment. Tenney and Rivenburgh recount their experience in the *serum treatment* of 68 cases of lobar pneumonia due to Type I pneumococcus. All the cases except four were in coloured soldiers. On admission, if lobar pneumonia was diagnosed or suspected, ½ c.c. of horse serum was given subcutaneously to desensitize the patient; thus some hours were saved. At the same time sputum was sent to the laboratory to be 'typed'. A blood count and on many occasions, a blood culture were done; the urine was examined and an X-ray examination asked for to check the physical findings. From four to six hours after admission the first dose of serum was given. This caused slight if any change in the blood picture. Slight anaphylaxis occurred three times. A thermal reaction, comparable with that which so often follows the intravenous injection of any foreign protein, showed itself in only a few instances. This reaction was always favourable, and several times resulted in a prompt crisis. Serum sickness, coming on from four to sixteen days after the last injection, was seen in practically all the cases treated; but the symptoms of urticaria or asthma were relieved by a hypodermic injection of 0·5 to 1 c.c. of epinephrin in a 1:1,000 solution.

The serum was administered in 100 c.c. doses and given at body temperature every eight hours night and day until the rectal temperature registered 100° or lower, or until signs of impending death appeared which made it wiser to desist. 61 of the 68 patients received antiserum in amounts varying from 30 to 900 c.c. with an average dose per patient of 344 c.c. Of the seven who received no serum, 6 were already convalescent when the sputum was typed, and the sputum of the remaining one showed Type IV pneumococcus and *B. influenzae.* At the autopsy on this last case Type I alone was recovered from the heart's blood.

Thirty of the 61 patients recovered by crisis, 22 by lysis, and 9 died. In addition to the serum treatment, abundant fresh air was afforded and digitalis and whisky were given in the critical stage, and codein as a sedative if necessary. Workers at the Rockefeller Institute place the mortality in Type I pneumonia cases, who do not receive antiserum (Type I), at 25 per cent., and in a series of 101 treated cases the mortality was only 7·5 per cent. The mortality in the series of Tenney and Rivenburgh was 14·7 per cent. This higher rate may be due partly to the lower resistance of coloured people towards pneumonia, to the season of the year (February to March 1919), and to the forced moving of the patients at the beginning or early in the course of their illness. The authors give a comprehensive table of their cases.

Cohen treats all his cases of pneumonia with *quinine*; using the dihydrobromide by mouth, quinine and urea hydrochloride for intramuscular injections, and for intravenous therapy either of these or the dihydrochloride. The drug is not given to reduce the temperature, but the degree to which this is lowered is taken as an index of the extent of the pharmacological action of quinine. Cohen states that the bactericidal properties of the blood of cinchonized animals and men and the power to prevent growth of cultures of pneumococcus *in vitro,* are retained much longer if the quinine is given in frequent small doses than if given in larger ones at greater intervals. Cohen keeps the temperature down to 100° or less; by mouth 25 to 35 grains are given at once, and later 5 to 15 grains every 2, 3, or 4 hours to bring about the desired effect. Quinine thus given, he says, is extremely well tolerated by pneumonia patients, but is very toxic if prescribed internally in the form of optochin (ethylhydrocuprein). The latter drug is very useful for local applications in pneumococcal infections. Intramuscularly 20 to 25 grains of quinine are given, and this may be continued daily with doses by mouth of 5 to 15 grains every 3 hours in addition. Intravenously Cohen gives 10 to 15 grains in 100 c.c. of normal saline and sometimes no further quinine is necessary, but should the temperature rise again, 5 to 15 grains by mouth every 4 hours are prescribed.

Cohen highly recommends the use of *pituitary extract* (posterior lobe) in subcutaneous doses of 1 c.c. every third hour until the systolic blood-pressure in millimetres of mercury exceeds by five points the number of heart-beats per minute. He emphasizes the virtues of this and also of *eserin* in the treatment of tympanites. He employs *digitalis* to sustain the diastolic blood-pressure; the outlook in a case of pneumonia being unfavourable if this pressure, expressed in millimetres of mercury, is within less than ten points of the rate of respirations per minute, or if it falls below 60 (irrespective of the respiratory rate) before the fever has ceased.

From the outset he prescribes 5 minims of a good tincture three times a day, and if the diastolic blood-pressure falls the drug is given in larger amounts every four hours. He has often noted little change in the pulse-rate or systolic blood-pressure in cases of pneumonia, although digitalis caused an increase in the diastolic pressure.

Sterling makes a plea for the early use of *atropin* in pneumonia, pointing out that unfavourable reports as to the efficacy of the drug are due to the fact that it is often begun too late, when signs of vasomotor collapse and oedema of the lungs are already present. He quotes a number of descriptions, given by various writers, of the condition of the lungs found in influenzal pneumonia. A very 'wet' lung was a frequent finding. Just as it has been found of value to digitalize the heart early in pneumonia, so he advocates the administration of atropin in influenza, even before signs of pneumonia are present. Sterling gives it hypodermically in doses of gr. 1/150 to 1/100, or 5 to 10 drops of a tincture of belladonna. He lost only 8 cases out of 120 of clinically definite pneumonias, and 2 of these were moribund at the first visit. His success, it appears, might as easily be ascribed to pituitrin and to digitalis, which were used all though the illness.

Weaver gives *sodium citrate* in pneumonia and employed this treatment in 47 cases, some of which were very severe. In 45 of these the duration of disease was decreased and a quick defervescence by crisis or by rapid lysis was brought about. This effect was produced in 48 hours up to 4 days. One of the unsuccessful results was in an alcoholic of 65 years of age, and the other case was that of a woman aged 91. According to Weaver, the *sine qua non* for a cure in pneumonia is the re-establishment of the cardio-pulmonary circulation in the hepatized lung, and this sodium citrate helps to do by decreasing the coagulability of the blood, which is always increased in pneumonia. Sodium citrate also helps to maintain the alkalinity of the blood. It is given to adults every hour, day and night, with an abundance of water, in doses of from 0·9 to 1·2 grm. or 2·4 grm. every 2 hours. Even larger doses are necessary sometimes. Should diarrhoea result, a mild opiate is indicated. This form of treatment is claimed to be especially efficacious in frank lobar pneumonia and also in cases of influenzal broncho-pneumonia. Vivaldi reports two patients successfully treated in this way.

In 50 cases of pneumonia caused by Friedländer's bacillus *optochin* was found by Zander to be of no avail. This stands in marked contrast, he says, with cases due to the pneumococcus so treated. Experiments on animals and those carried out *in vitro* showed that the drug did not inhibit the infection and growth of the organism. In spite of the severity of the infection, no cases treated with optochin exhibited secondary ill effects.

Pearl applies statistical methods in judging the results published by G. D. Head ('Treatment of Pneumonia,' *J. Am. M. Ass.* 1919, **72**, 1268), which seemed to show that there were fewer deaths from post-influenzal pneumonia treated by the closed ward method than by treating the patients with fresh air outside. The questions which Pearl tries to answer are: Whether the lower mortality was just a coincidence, such as may appear in any cases chosen at random; whether a lower mortality would naturally be expected towards the end of an epidemic wave, when the disease is subsiding; or finally, whether it was due to an improved method of treatment. In Head's series at Camp Wheeler, out of 966 cases of pneumonia treated outside 135 died, whilst later in the epidemic, only 14 died of the 435 cases treated in a closed ward. On the theory of probability, we should expect that 61 patients would have died during the latter period, if the factor of decrease in severity of disease and change of treatment were not taken into account. But there were only 14 deaths, or only about 23 per cent. of those which would be expected under the conditions above assumed. Pearl now compares these figures with those at Camp Pike, where open-air treatment was carried out all through the epidemic wave of the autumn of 1918. Pearl divides the series of epidemic cases there at a point which corresponds proportionally with the time at which the treatment at Camp Wheeler was changed from the fresh air to the closed ward type. In the first period there were 1,004 cases and 364 deaths. In the second period of 499 cases, if the proportion of deaths had persisted, we should expect 182 deaths, but there were only 77, or a mortality of 42 per cent. of those expected. So at Camp Wheeler with the closed ward treatment the deaths were only 23 per cent. of those expected in the second period, whilst at Camp Pike they amounted to 42 per cent. of those we should anticipate. This difference Pearl states, when both epidemics were statistically considered in exactly the same way, must be due to difference in treatment at the two camps. It would seem, however, that Pearl assumes that the epidemics of influenza at these two camps decreased in severity at proportionally the same rate, and in this assumption he is perhaps not justified.

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A. M.

SCARLET FEVER

Aetiology. The question of susceptibility to scarlet fever is discussed by Rominger, assistant in the Freiburg University Children's Clinique, in which two outbreaks recently occurred. On both occasions it was children of a more or less marked lymphatic constitution who proved most susceptible. The patients in question were normally developed, vigorous, and often overfed children, or else examples of severe scrofula with evidence of lymphatism. Patients with varicella appeared to be particularly susceptible. On the other hand, infants under six months escaped, even when suffering from varicella, and among the older children immunity appeared to be possessed by those who were below normal weight, puny, and of poor glandular development, even when their skin was liable to other infections. Rominger concludes that there is a connexion between the contagium of scarlet fever and the lymphatic system, the evolution of which occurs at that period of life which is most susceptible to scarlet fever. A certain degree of protection against the disease appeared to be afforded by abundance of skin pigment and possibly also by the administration of cod-liver oil.

Symptomatology. According to Brelet, *endocarditis* is a rare complication of scarlet fever, in spite of the contrary opinion expressed by Bouchut and the older writers, who regarded it as frequent, because they did not recognize the existence of extracardiac murmurs, which are very common in scarlet fever in children. The complication may or may not be associated with scarlatinal rheumatism, and is very liable to escape notice. In rare instances in which it is infective and ulcerative it may prove fatal. As a rule it is mild and non-infective, though it rarely ends in complete recovery. In most cases a chronic valvular lesion is established. Pericarditis may occur alone or in association with endocarditis. It is usually latent and generally subsides rapidly unless it is purulent, when it is almost always fatal. Functional disturbance of the myocardium, which is not necessarily accompanied by definite anatomical lesions, is of more interest. In ordinary cases tachycardia at first is so frequent that it has some diagnostic value. In malignant cases it is extreme, the pulse being 160, 180, or 200, and accompanied by marked arterial hypotension. But sometimes there is a more or less pronounced bradycardia which is fairly frequent in adolescents and adults, though very exceptional in the child. It occurs chiefly at the end of the febrile period, and lasts from 18 to 20 days, the pulse being on the average 56, but sometimes as low as 40 or 42. According to Monier-Vinard and Meaux-Saint-Marc it is a total bradycardia of nervous origin without auriculo-ventricular dissociation, and the prognosis is not unfavourable. Cardiac disturbance in scarlatinal nephritis is often an early and predominant phenomenon, the clinical picture being that of cardiac rather than of renal disease. Cardiac dilatation which may be of considerable degree is produced by the sudden rise of blood-pressure. Gallop rhythm is almost constant.

In discussing the *respiratory complications* of scarlet fever Brelet states that involvement of the larynx may occur in the course of ulcero-membranous angina. In some cases there may be merely a transient functional disturbance such as slight hoarseness and some degree of laryngeal irritation, while in other cases the symptoms are more serious. Broncho-pneumonia is not a very rare complication of scarlet fever. According to Gouget it occurs in 16·43 per cent. of all fatal cases. It is often overlooked because it occupies a secondary place in the clinical picture. It occurs chiefly in very young children. It may be transmissible and contagious, affecting several children in the same ward. In most cases it succeeds a severe infection in the upper part of the respiratory tract, such as suppurative rhinitis, or infection of the naso-pharynx, and is most likely to be met with in children whose nasal respiration is insufficient owing to adenoids, thickened Schneiderian membrane, or narrow nasal fossae. It is frequently found when scarlet fever is complicated by measles. In rare cases lobar pneumonia may occur at the onset of scarlet fever, before or shortly after the appearance of the eruption. When it appears late it is usually in association with nephritis or due to an intercurrent infection. Pleurisy occurring in scarlet fever or in convalescence varies in its origin and character. Thus it may be (1) infective or septicaemic, (2) associated with endopericarditis and scarlatinal rheumatism, (3) sero-fibrinous pleurisy with effusion occurring in convalescence. It is then to be regarded not as a complication but as a tuberculous pleurisy, the sequel of scarlet fever. Although scarlet fever does not predispose to tuberculosis like measles or whooping cough, it is a mistake to suppose with Rilliet and Barthez that the two diseases are naturally antagonistic, as scarlet fever may sometimes be followed by acute miliary tuberculosis.

Meurisse, of Nice, records a case in a boy aged 14 in which the onset of scarlet fever was accompanied by well-marked obstructive *jaundice.* He attributes the condition to a simple angiocholecystitis with an abundant exudation in the bile canaliculi. The rapidity of its development and the negative results of a blood culture were against the possibility of the condition being due to an ascending microbial infection.

According to Canelli, of Turin, who records a fatal case in a child aged 2 years, *appendicitis* is a rare complication of scarlet fever, only 15 cases having been recorded in literature. In Canelli's case symptoms of appendicitis developed on the sixth day of a severe attack of scarlet fever complicated by endocarditis, and death took place without operation on the eleventh day. The necropsy showed acute muco-purulent tonsillitis, acute sero-fibrinous pericarditis, acute endomyocarditis with recent verrucose endocarditis of the mitral and tricuspid valves, and acute catarrhal inflammation of the appendix from which a virulent streptococcus was cultivated.

From examination of 17 cases of simple scarlet fever, and of 2 cases complicated by *nephritis*, Veeder and Johnston found that although the functional changes occurred in nephritis and paralleled fairly closely the urinary changes, the albumin appeared in the urine before the changes in renal function took place. They conclude that as a routine measure the examination of the urine for albumin is of more value than the functional tests in announcing the onset of nephritis.

Blood. Schiff and Friedemann, of Buda Pesth, investigated the haemoglobin content of the blood and the number of the red corpuscles in 34 cases of scarlet fever of various degrees of severity with the following results. The haemoglobin content was diminished during the early days of the disease, but no connexion was found between the initial haemoglobin content and the intensity of the eruption. In 14 cases there was a fall in the number of the red corpuscles after the temperature had become normal, in 16 at the end of the febrile stage, and in 4 in spite of the presence of febrile complications. The extent of the fall varied and showed no relation to the severity of the case. It appeared, however, to have some connexion with the height of the fever. In cases in which there was only a moderate degree of fever in the acute stages the number of the red corpuscles did not fall so low as in cases with a high temperature. In most cases normal red cell counts were found again within 30 days. In the majority of cases, however, regeneration of haemoglobin occurred later than the return of the number of the red cells to normal. Even at the end of the sixth week only one-third of the cases examined showed normal or approximately normal haemoglobin values ; in the other two-thirds subnormal values were found.

Schiff and Mátyás investigated the blood-platelets and coagulation of the blood in 16 cases of scarlet fever. In 10 normal counts were found at the height of the eruption; in 3 they were considerably increased, and in 1 diminished. As the eruption faded a considerable increase in their number occurred in 14, and in only 1 case was there a diminution. The fever did not appear to have any effect on the number of the platelets. The bleeding and coagulation time was usually shortened. The retractility of the clot was always normal.

The following description of the condition of the leucocytes in scarlet fever is given by Türk, of the Frankfort Children's Clinique, who examined the blood in 48 cases in children aged from 2 to 5 years. In the first few days of the disease there is a moderate leucocytosis with a relative increase of the neutrophil leucocytes. A slight increase in the number of the leucocytes persists throughout the disease and becomes more marked as late as the sixth week. Eosinophilia reaches its height at the fifth day, but never completely disappears throughout the disease, being still pronounced in the fifth and sixth week. In complicated cases eosinophilia is most marked between the eighth and tenth day.

The Wassermann reaction in scarlet fever. It is frequently stated that the Wassermann reaction may be positive for a short time in scarlet fever. Some writers report positive reactions in half or even more of their cases. Boas, however, who collected statistics from various sources, found only 29 positive reactions among 617 cases of scarlet fever. Loederich and Bory, from whose paper this information is taken, investigated the Wassermann reaction in 20 cases of scarlet fever at various stages of the disease with antigens of various degrees of sensitiveness. The results were as follows: With a very sensitive antigen the reaction was constantly positive during the first few days of the disease, and then became rapidly and progressively negative, whereas with antigens which were only moderately or slightly sensitive the reaction was almost always negative throughout the disease. The character of the reaction showed no relation to the gravity of the disease or to the severity of any particular symptom. These findings appear to explain the differences in the results recorded by various observers.

Scarlet fever and vaccinia. Jonesco records a case showing that scarlet fever not only does not prevent the regular development of vaccination, but even appears to increase the receptivity of the organism for the vaccine virus. His patient was a woman who had been vaccinated unsuccessfully at the age of 1, 8, and 15 years, although vaccination of her brother at the same time and with the same lymph proved successful. At the age of 23 she was vaccinated at the end of the incubation period of scarlet fever, and three days later the vaccine lesions began to develop and pursued their normal course with all the local and general symptoms of primary vaccination. The attack of scarlet fever was one of moderate intensity without any complications, and convalescence was uneventful. It was, therefore, in no way affected by the concomitant vaccinia. On the other hand, the attack of scarlatina appeared to have rendered the organism more susceptible to the vaccine virus.

Isolation and return cases. Hitherto the determination of the period during which convalescents from scarlatina are infectious has been more or less empirical. In Denmark it has been the orthodox practice for many years to isolate these convalescents for eight weeks. In Christiania the minimum period of isolation is six weeks. In Stockholm this period is extended to seven weeks. In France it is usually 40 days. Germany and Austria allow six weeks. The extremes range from four to eight weeks—a wide difference which is the measure of the lack of reliable data on the subject. Since his appointment, on October 1, to the Blegdam Hospital, where for many years eight weeks had been the minimum period of residence in hospital, Bie has gradually reduced this period. In May 1916 residence in hospital was reduced to 42 days, and in December of the same year a further reduction was made to 38 days. This was the minimum; severe cases and complications required longer hospital treatment. No ill effects of this reduction could be found either in the number of notifications of scarlatina in the district supplying the hospital or in the number of cases discharged from the hospital. The number of discharges in the years 1912, 1913, 1914, 1915 were 1,402, 1,239, 1,180, and 1,343. In the years 1916, 1917, 1918 the discharges numbered 1,107, 1,473, and 969. Defining a 'return case' as that of the patient admitted to hospital from a home to which another member of the family has been discharged, within four weeks, from hospital, the writer notes that out of 3,175 discharges between May 3, 1916, and December 31, 1918, there were 60 'return cases', i.e. 1·9 per cent. of the total. His predecessor, Sörensen, found the 'return cases' represent 3·6 per cent. of the total, although the minimum residence in hospital was 56 days. Though Sörensen's calculations referred to a nine-year period and 10,299 cases, whereas the writer's covered a period of only two years and eight months, he submits that his figures are big enough to justify a comparison. The comparatively low incidence of his 'return cases' may be due to more careful sifting of cases for discharge, patients with a discharge from the mucous membranes being kept longer in hospital than others. Another factor may be the comparative mildness of the cases in 1918. The writer also analyses the incidence of relapses and of the commonest complications, with special reference to the period at which they occurred. He found 26 cases of relapse and 10 of nephritis occurred between the 39th and the 56th day of the disease. These findings do not, however, warrant keeping 1,258 patients in hospital for 56 instead of 38 days. He concludes with an estimate of the saving of money and hospital accommodation effected by his reduction of the period of isolation, which he anticipates can be further brought down to 35 days.

Diagnosis. Paschen, of St. George's Hospital, Hamburg, has employed the diagnostic test introduced by Schultz and Charlton, which is carried out as follows: at the height of the eruption the patient is injected intracutaneously with 1 c.c. of convalescent or normal human serum, and in positive cases five to eight hours later an anaemic zone appears varying in size from that of a five-shilling piece to the palm of the hand. This phenomenon does not occur if recent scarlatinal serum is injected, nor after injection of normal horse serum, diphtheria antitoxin, or saline solution, nor is it present in measles or mercurial rashes. Among 71 cases of scarlet fever in which Paschen tried the test it was positive in 62 and negative in 9, but in the negative cases the serum was used too late or not injected strictly intracutaneously. Paschen concludes that the phenomenon is pathognomonic of scarlet fever, or at least is a valuable confirmatory test in the differential diagnosis. The serum is best taken from the convalescent at the beginning of the fourth week, tested for sterility and the Wassermann reaction, and kept in sterile ampoules till it is required. As regards the nature of the reaction Paschen suggests that the dilatation of the cutaneous vessels caused by the scarlatinal toxin becomes converted into vasoconstriction owing to a peculiarity of convalescent or normal human serum. The alarming symptoms, such as rigors and severe collapse, sometimes following intravenous injection of the serum of scarlet fever convalescents are attributed by him to sudden vasoconstriction.

The test was also carried out by Hainiss, assistant at the Hungarian University Children's Clinique at Pressburg, in 27 children with various rashes, which included 2 of serum eruption, 2 of erysipelas, and 4 of influenza, in all of which it was negative, and in 19 cases of scarlet fever, in 11 of which it was positive and in 8 negative.

In 64 cases of scarlet fever, in which Neumann of Hamburg employed the test, a positive result was obtained with very few exceptions, which might be attributed to the early fading of the eruption, whereas the result was negative in 3 cases of measles, 4 toxic scarlatiniform rashes, 1 urticarial erythema, 3 scarlatiniform serum rashes, and 1 scarlatiniform paratyphoid rash. The reaction did not occur with injections of non-human serum or with distilled water, normal saline, or adrenalin in various dilutions. Neumann points out that advantage may be taken of the fact that scarlet fever serum in the acute stage does not cause the rash to fade by injecting the serum of a suspected case, in which the rash is ill-marked or faded, into an undoubted case of scarlet fever with a well-developed rash. If this rash disappears as the result of the injection the doubtful case is not scarlet fever, whereas if the rash is not affected the diagnosis of scarlet fever is established. The value of the test, however, is diminished by the fact that injection of the serum of rubella patients also has no effect on the rash of scarlet fever. Moreover the necessity of first performing a Wassermann reaction and testing the serum for sterility before injection makes it doubtful whether the test will ever become widely applicable.

Müller, jun., assistant at the Zurich University Medical Clinique, investigated the Rumpel-Leede sign (appearance of petechiae at the elbow after constriction of the upper arm) in 116 cases of scarlet fever with the following results. Rapid and well-marked appearance of the sign was almost entirely confined to cases with a distinct and intensely red eruption. Consequently it was found much more frequently with a high temperature, and in the first five days of the disease, than with a low temperature and in convalescence. When the rash was faint or had faded the sign was slow in appearing and was ill-marked. Müller therefore concludes that it is of no diagnostic value in scarlet fever, but merely an indication of the strength of the eruption. The spontaneous development of petechiae accompanying a bright scarlatinal rash is also a proof of the connexion of the sign with the eruption. It is true that there is an increased tendency to skin haemorrhages in scarlet fever as compared with other diseases, but only when the eruption is well developed. When the rash has faded the tendency to petechial haemorrhages is not greater than in other diseases or in normal persons.

Prognosis. In a paper emanating from the department for infectious diseases of the Wilhelmina Hospital at Amsterdam, Duyvis reports the result of an inquiry into the subsequent history of 50 patients who had developed nephritis while under treatment for scarlet fever in the hospital in 1906. Of the 50 cases 30 were examined with the following results: 21 were found to be quite healthy; 4 had a raised blood-pressure with little or no albuminuria and a satisfactory general condition; 2 had intermittent albuminuria with normal blood-pressure and a good general condition; 1 had intermittent albuminuria with normal blood-pressure and a suggestion of tuberculosis; and 2 had albuminuria with normal blood-pressure and a good general condition. Duyvis concludes that the general rule in infectious diseases—death or recovery—does not apply to scarlatinal nephritis, though the second alternative appeared to be more true than the first, since after 10–12 years none of the cases showed a fully-developed nephritis, and none had died.

Treatment. Griesbach, of the Wiesbaden Municipal Hospital, carried out the treatment introduced by Reiss and Jungmann by intravenous injections of convalescent serum in 21 cases, except in two in which normal human serum was used. The Wassermann reaction and the sterility of the serum were tested in each case before use. Although in the majority of cases the results were satisfactory, as was shown by a rapid fall of temperature and recovery, severe and often dangerous complications occurred. In 8 cases the injection was followed by rigors, and in 4 of these by severe collapse, and in another 2 death took place from heart failure from 3½–4 hours after the injection. No autopsy was permitted in either case. Commenting on Griesbach's article Reiss states that since 1911 182 cases of scarlet fever have been treated at the Frankfort Municipal Hospital with convalescents' serum and 39 with normal human serum. True collapse was very rare, and was easily remedied by ordinary stimulants. No severe or fatal cases occurred. Much larger doses were used than Griesbach's 10 c.c., viz. 50 c.c. for children and 100 c.c. for adults. Reiss attributes Griesbach's unfortunate results to the manner of preparation of the serum, and possibly to a different method of administration. Individual hypersensitiveness could also not be excluded.

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SYPHILIS

Pathology. In his article on 'Normal and Morbid Conditions of the Testes from Birth to Old Age', Mott describes **the influence of syphilis on the germ cells.** He states that in 50 cases of general paralysis in which an emulsion of the testicles was examined for spirochaetes, these were never found, while they were present in emulsions of the brain in 66 out of 100 cases. This indicates that the seminal fluid of a general paralytic is probably non-infective at the time of this disease. General paralysis does not usually develop till ten years after infection, so that if the infected man does not marry till five years after infection, he is not likely to infect his wife, and he may procreate healthy children, in spite of the presence of spirochaetes in his brain, and a positive complement reaction in his blood and cerebrospinal fluid. Mott suggests the possibility of the spirochaetes of general paralysis and tabes having a biological disposition to enter the brain and spinal cord, where they can exist in the tissues and cerebrospinal fluid away from the attacks of leucocytes and spirochaeticidal agents such as mercury and arsenic. Inoculation of the testicles of monkeys with tissue containing spirochaetes from the brains of general paralytics was negative (Förster and Tomasczewski).

Examination of the semen of general paralytics showed both normal and degenerate spermatoza, but in no case did the semen show such deficiency in numbers or such degenerate forms as the semen in cases of dementia praecox. Hence, an acquired dementia due to the direct action of the toxins of the spirochaetes of syphilis on the brain does not cause arrest of spermatogenesis. Mott concludes that, while the degenerative changes in the brain in general paralysis are due to chronic inflammatory reaction caused by spirochaetal toxins, dementia praecox is a primary nuclear degenerative process with no inflammatory reaction and no obvious naked eye changes in the brain.

Syphilis in the parents may cause *infantilism* in the offspring. These cases of infantilism may show no signs of congenital syphilis, but other children of the same parents often do so. Examination of the testes in cases of infantilism shows disappearance of the interstitial cells, which is held to be the cause of failure in development of secondary sexual characters. Mott thinks it more likely that infantilism is due to chronic spirochaetal intoxication depressing the vital energy of the whole body than to actual invasion of the testes by spirochaetes.

Cases of congenital syphilitic dementia paralytica, or juvenile general paralysis, show the same changes as those met with in the paralytic dementia of acquired syphilis: the presence of spirochaetes in the brain and signs of active spermatogenesis. Hence these cases are capable of procreating, but Mott has only observed one case in which the disease was transmitted to the third generation.

Fischl discusses the question of the **organotropic action of the Spirochaeta pallida.** He mentions the well-known instance of Brosius' seven glass-blowers, infected with labial chancres from the same source, five of whom developed tabes and two general paralysis; also, Morel-Lavallée's cases of five men infected from the same woman, one of whom developed syphilitic meningitis, two general paralysis, and one syphilitic psychosis, as evidence of a biological variant of *Spirochaeta pallida* possessing special neurotropic power. He then reports three cases of icterus, which he thinks may be explained by a special hepatotropic action of the spirochaete. In the first case, a woman, icterus developed suddenly after a complete course of salvarsan and mercury, and disappeared under further treatment of the same kind. The second case, husband of the first, is stated to have had jaundice, which appeared and disappeared before antisyphilitic treatment was commenced. The third case, a woman from whom the husband contracted syphilis, is stated to have had jaundice during mercurial treatment. Fischl is of opinion that the icterus developing in these three patients, all infected originally from the same source, one after salvarsan and mercury, one during mercurial treatment, and one without any treatment, suggests a possible hepatotropic power in certain spirochaetes.

Syphilis and Tuberculosis. The accelerating action of acquired syphilis on tuberculosis in evolution, and, on the other hand, the retarding influence of a fibrous soil prepared by tertiary syphilis on the progress of tuberculosis are well known; but the influence of heredo-syphilis on tuberculosis and the beneficial effect of mercury in this symbiosis are not so well known. Marino and Mussio-Fournier have observed many cases of pulmonary tuberculosis (proved by presence of Koch's bacillus) which were considerably improved by mercurial treatment, which they administered in small doses in every case when there was a probable history of syphilis in the parents, even if there were no signs of heredo-syphilis present in the patients. In these cases pure antituberculosis or pure antisyphilitic treatment generally failed, but combined treatment by fresh air, sunlight, arsenic, iodine, tuberculin in small doses, and mercury carefully given produced good results. As to the frequency of this symbiosis the authors remark that this is at present unknown, but they are of opinion that a large percentage of affections of the lymphatic type, and those of the endocrine glands are of heredo-syphilitic origin.

Symptomatology. Queyrat draws attention to the **absence of the xiphoid process** as a sign of heredo-syphilis. As an example, he reports the case of a girl of 14, with interstitial keratitis and a positive Wassermann reaction, in whom the xiphoid process was absent. He also mentions the frequent association of absence of the xiphoid process with congenital mitral stenosis, which he considers to be of heredo-syphilitic origin.

Syphilis of the lung. Carrera has examined the lungs from 152 cases in which the diagnosis of syphilis was made from the presence of undoubted syphilitic lesions in other organs. One-third of the cases had been clinically diagnosed before death (cerebral, cardiac, aortic, and hepatic syphilis, and 5 cases of death after salvarsan), the diagnosis in the rest depending on the finding of the spirochaete or other signs of syphilis. In only 12 cases were definite histological lesions of syphilis discovered, but Carrera attributes this small proportion to the fact that the parts examined represented only a small area of the lung, and is of opinion that the lungs are probably affected in the same proportion as other organs. The 12 cases included 3 of gumma, 2 of peribronchitis with arteritis, 4 of fibrosis with arteritis, and 3 of arteritis only. As regards differential diagnosis, he points out that gumma differs from tubercle in its gradual transition into the surrounding tissues, and in leaving ramifying scars; that syphilitic fibrosis is characterized by extension along the vessels and bronchi, and by the presence of plasma cells; and that tuberculous arteritis affects all coats of the vessel equally, while in syphilitic arteritis the middle coat often escapes. He draws attention to the frequency of other pulmonary lesions, especially brown induration, in this series, which he thinks was secondary to syphilitic myocarditis.

Syphilis of the bladder. Thompson has collected 84 cases from the literature of reported syphilis of the bladder, only 58 of which he considers authentic, including one personally observed. In this case, a man of 25, with early secondary syphilis, untreated, the symptoms were frequent micturition and haematuria, and the presence of red blood cells, leucocytes, and bladder epithelium in the urine. Cystoscopic examination showed hyperaemia of the mucous membrane and several ulcerated papules near the orifice of each ureter, resembling mucous patches. Examination of the urine was negative for spirochaetes. All symptoms disappeared after four weeks' treatment with arsphenamin and salicylate of mercury. The collected cases varied in age from 4 to 71, and there were 37 males to 21 females. The pathology in early syphilis is the same as in the author's case. In later syphilis, gummas, single or multiple, ulcerated or non-ulcerated, have been reported. Perforation into the peritoneum and rectum has been recorded. The chief symptoms are frequent and painful micturition, haematuria, pain in the perineum and glans penis. The diagnosis depends on the history, the presence of other signs of syphilis, the Wassermann test, and the effect of treatment.

Congenital syphilis in orthopaedic clinics. Roberts, from his experience in orthopaedic clinics during the last few years, comes to the conclusion that recognition of the prevalence of inherited syphilis and its potency in producing disabilities of function would often eliminate the necessity for surgical or mechanical treatment. The cases he observed were 81 joint conditions simulating tuberculosis; 14 cases of osteomyelitis of the long bones; 5 cases of torticollis; 12 cases of myotonia; 5 cases of adenitis supposed to be tuberculous; 17 cases of myositis; 24 cases of arthritis; 8 cases of carpal and tarsal disease; 10 cases of osteochondritis of the hip; 33 cases of spinal caries; and 1 of lateral curvature. All these cases presented some evidence of inherited syphilis, and all responded to antisyphilitic treatment. The Wassermann test was not found of much assistance, as negative reactions occurred where the family history was positive and the lesions yielded to mercury and iodide. This is said to be a frequent occurrence when symptoms of inherited syphilis do not appear till some years after birth. The most interesting results were obtained in lesions of the spine and large joints, where the symptoms were identical with those of tuberculosis, and in many of which this had been diagnosed by orthopaedic surgeons and treated by the usual method of immobilization. Of these cases 114 were improved after two or three weeks of antisyphilitic treatment, and most cases in which the large joints were affected became free of symptoms in two to six months. As relapses may occur, treatment should be continued for at least a year. Five cases of torticollis were relieved by this treatment, including one case of congenital wry neck, which had been operated upon three times unsuccessfully. In this case the child had Hutchinson's teeth and a positive Wassermann reaction.

Roberts concludes that many syphilitic cases are unrecognized in orthopaedic clinics, because of the tradition that nearly all chronic lesions of the spine and large joints are tuberculous, and also because the far-reaching distribution of congenital syphilis is ignored.

Neurosyphilis. The clinical value of **changes in the cerebrospinal fluid** in syphilis has been investigated by Van der Valk. The number of cases examined was 250, and these were divided into 7 groups—primary, primary and secondary, secondary, latent secondary, tertiary, quaternary, congenital. Out of 49 cases of primary syphilis the cerebrospinal fluid showed changes in 8, the Wassermann reaction being positive in 2, and the Nonne reaction in 5, the latter reaction thus proving the more sensitive. In 1 case, a chancre of 7 days' duration, there were changes in the cerebrospinal fluid while the blood was still negative. This furnishes evidence in favour of the occurrence of general infection of the body before the blood becomes positive, and agrees with the experimental evidence obtained from monkeys by Neisser, who found spirochaetes in the internal organs even before the development of the primary sore. Another case was remarkable for the development of alopecia and pigmentary syphilide of the neck in connexion with a chancre of four weeks' duration.

Out of 31 cases of primary and secondary syphilis there were changes in the cerebrospinal fluid in 9. Here again the Nonne reaction was the more sensitive, and lymphocytosis was more frequent than in the first series. One case was noteworthy in the early occurrence of syphilitic polyneuritis before the outbreak of secondary eruptions. Van der Valk does not support Benario's view that the central nervous system is rapidly invaded by spirochaetes in cases of primary chancre of the head, for in 7 such cases (4 chancres of the tongue, 1 of the conjunctiva, and 2 of the gums) he found no changes in the cerebrospinal fluid.

Out of 118 cases of secondary syphilis changes were present in the cerebrospinal fluid in 42. The Wassermann reaction was positive in 17 cases, the Nonne reaction in 31, and 36 showed lymphocytosis. There was no parallelism between the degree of these three phenomena. Two cases with the so-called 'neuro-recurrence' were remarkable in having a negative Wassermann reaction in the blood.

From Van der Valk's experiences the secondary period of syphilis furnishes many cases of early meningitis, which, although they do not present the normal characters of meningitis, may be recognized by certain symptoms. The chief of these are severe headache; insomnia or somnolence; subjective labyrinthine symptoms, such as noises in the ears, vertigo, and slight deafness; visual troubles, including optic neuritis. According to Van der Valk acneiform and lichenoid syphilides are often accompanied by meningitis; also iritis, which he regards as a symptom of early meningitis. Changes in the cerebrospinal fluid were also common in syphilitic leucodermia and alopecia, thus supporting the view that these lesions are of a neurotropic nature.

Out of 22 cases of latent secondary syphilis, 7 showed changes in the cerebrospinal fluid. The Wassermann reaction was positive in 2, the Nonne reaction in 6, and lymphocytosis was present in 2.

Out of 20 cases of tertiary syphilis, 9 showed changes in the cerebrospinal fluid. The Wassermann reaction was positive in 7, the Nonne reaction in 6, and lymphocytosis was present in 4. Hence in the tertiary period the Nonne reaction ceases to be the more sensitive.

In 5 cases of quaternary syphilis (3 of tabes and 2 of taboparalysis) changes in the cerebrospinal fluid were found in all. A comparison of the tables of cases of tertiary and quaternary syphilis shows that in the former no index in the cerebrospinal fluid is above that of the blood, while in the latter group all indices in the cerebrospinal fluid are higher than those of the blood.

According to Van der Valk, this indicates that when syphilis attacks the nervous system in the form of tabes and paralytic dementia, the nature of this quaternary syphilis is different from that of the tertiary period. Patients with gummatous lesions, even of the central nervous system, appear to be exempt from tabes and paralytic dementia. He holds the view that syphilis which is originally malignant is not followed by tabes and paralytic dementia, but that these conditions follow syphilis which is originally benign. The most critical period, he remarks, for the future of the patient is the latent secondary period, during which the disease may diverge to tertiary syphilis or to quaternary.

In 5 cases of congenital syphilis, 3 with active symptoms and 2 with stigmata, no changes were found in the cerebrospinal fluid, but 4 gave a positive Wassermann reaction in the blood. Changes in the cerebrospinal fluid have been found by others in cases of congenital syphilis, and Van der Valk attributes the negative results in his cases to the fact that all but one were adults and past the age of juvenile tabes and dementia.

Klauder reviews the subject of **early neurosyphilis.** He points out that, although several observers have reported changes in the cerebrospinal fluid in primary and secondary syphilis, they differ widely in their findings. This is partly explained by the divergence in standard of lymphocytosis; the normal lymphocyte content of the cerebrospinal fluid adopted by different observers varying as much as from 1 to 10 lymphocytes per cubic millimetre.

Some observers consider that slight changes in the cerebrospinal fluid, such as an increase of a few cells and a trace of globulin, represent only transient meningeal irritation and are not sufficient evidence of syphilitic involvement of the nervous system. They hold that those only who show more marked changes are candidates for cerebrospinal syphilis, and estimate the number of these at 10 per cent., which closely agrees with the stated percentage of syphilitics who later develop clinical neurosyphilis. Of importance are the finding of the *S. pallida* in the cerebrospinal fluid in primary and secondary syphilis and positive inoculation of apes with cerebrospinal fluid.

In these positive cases the spinal fluid was otherwise normal in some and abnormal in others; subjective symptoms were sometimes present, sometimes absent; the serum Wassermann reaction was sometimes positive, sometimes negative. Hence there was no regularity in the findings apart from the presence of the *S. pallida* in the fluid. Also in late neurosyphilis the *S. pallida* has been found by several observers, in some cases without other changes in the spinal fluid.

Klauder thinks it reasonable to assume that the nervous system may react to early implanted foci of spirochaetes. This view is supported by clinical observation showing the effect of trauma, infectious diseases, or emotional stress and strain as exciting causes of paresis.

Klauder expresses the belief that at the time of generalized infection the nervous system is involved by the spirochaete probably in all cases of syphilis, but that the nervous system may or may not react to the organism. In early neurosyphilis the involvement may be meningeal, vascular, or parenchymatous; the meningeal type is the most frequent and may be divided into four groups: (1) with symptoms of acute cerebrospinal meningitis;

(2) with symptoms of acute psychosis; (3) with headache; (4) an asymptomatic group with signs in the spinal fluid of meningeal involvement, but no clinical symptoms. Types 3 and 4 are much the commonest, and Type 4 shows the necessity of examining the cerebrospinal fluid for diagnosis. As regards the cranial nerves, he remarks that the eighth is the most frequently affected in early neurosyphilis, in most cases both divisions, the cochlear and vestibular, being involved, and the involvement is usually bilateral. Next in order of frequency to be affected are the second, seventh, third, fourth, fifth, and sixth.

Treatment. In the First Report of the Special Committee upon the manufacture, biological testing, and clinical administration of **salvarsan,** it is interesting to note that the synthesis of this drug is only normal up to a certain point, after which no chemically pure substance can be isolated. Neither the base 592 nor the hydrochloride 606 can be crystallized, but are thrown out of solution in an amorphous condition, together with a variable amount of impurities, of which little is known. However, the Committee find no evidence that variations in toxicity, apart from those due to exposure to air, are due to toxic impurities. But they find evidence that the different toxicity of different samples is due to variations in the product itself. There is no definite chemical or physical test for these variations, the only test being the biological test on animals. However, they suggest the following tests to guarantee the identity, reasonable purity, and absence of artificial dilution or fraudulent substitution.

Salvarsan should be a pale yellow, dry, and amorphous powder freely mobile on glass surfaces, and free from odour except that due to traces of ether. The ash after ignition should not be more than 0·5 per cent. As regards solubility, 0·5 grm. should dissolve in 35 c.c. of distilled water when well shaken. The solution should be neutral to Congo red paper, of a pale yellow colour and perfectly clear. The addition of 1 c.c. of 15 per cent. sodium hydrate to the aqueous solution should precipitate the arsenic base, which should redissolve on shaking. This, diluted to 250 c.c. with 0·5 per cent. saline solution, should give a clear yellow liquid. The percentage of arsenic should not be less than 30 nor more than 34.

Neosalvarsan should be a yellow or orange powder forming a clear neutral solution with 0·6 grm. in 1 c.c. of distilled water. The percentage of arsenic should not be less than 18 nor more than 21.

For biological testing the mouse is the most suitable animal. For 606, the dose, injected intravenously in 1 or 2 per cent. alkaline solution, is 0·125 mgm. per grm.; for 914, 0·3 mgm. per grm. Five animals should be used, and if more than two die the sample should be rejected. One death in five is not considered sufficient for rejection.

As regards the administration of 606 and 914 (which terms are used for brevity to designate all preparations of the salvarsan and neosalvarsan types respectively) the Committee find no evidence to support oral or rectal administration. They find, however, evidence that intramuscular injections are more effective than intravenous, but objectionable owing to the pain they cause. Solutions of 606 should not be more concentrated than 0·3 or 0·4 grm. in 100 c.c.; stronger solutions may cause venous thrombosis or vasomotor troubles. Solutions of 914 may be concentrated to 0·9 grm. in 10 or 5 c.c. The doses recommended are 0·3 grm. for 606, and 0·45 for 914, as initial doses. No difference as regards effectiveness was found between British, French, and the original German preparations, but galyl is considered less effective in ordinary doses. Treatment by salvarsan alone is not recommended; this should be supplemented by mercury.

As regards the **ill-effects** of salvarsan, the Committee conclude that these may be due to (1) toxicity of the drug; (2) errors in technique; (3) susceptibility of the patient; (4) causes unknown. They state that vasomotor phenomena only occur after intravenous injections. These are normally slight, but may be severe, constituting the so-called 'anaphylactoid' or 'nitritoid' crises, manifested by flushing, swelling of the lips and tongue, cyanosis, and dyspnoea. They find that these occur after the use of too concentrated solutions of 606, or imperfectly dissolved 914, and consider that they may be due to the state of dispersion in which the colloidal drug circulates in the blood.

Early reactions, headache, fever, and rigor, occurring within 24 hours, are considered to be due to contamination of the water by dead bacteria, and are to be avoided by sterilizing the water after distillation. The liberation of endotoxins as a cause of early reactions is negatived by the same symptoms occurring in patients not infected with any organism upon which salvarsan is known to act.

Later reactions, headache, insomnia, malaise, and loss of weight, occurring after later injections, are attributed to intolerance of the drug. Cerebral symptoms, manifested by headache, convulsions, coma, and death, from 1 to 5 days after injection, are rare and appear to be connected with the dose and intervals between injections. The same applies to dermatitis and jaundice. Neuro-recurrences are considered to be clinical relapses of meningeal syphilis caused by insufficient treatment with 606. It is suggested that one or two doses destroy the spirochaetes in the skin, mucous membranes, and blood, but that the less accessible spirochaetes in the meninges may not be reached, and, unchecked by the presence of immune bodies in the blood, may cause more damage than usual. Treatment by larger doses of 606 and mercury is recommended.

The conditions given as indicating caution in the administration of 606 are as follows: (1) haemophilia, Graves's disease, Addison's disease, and lymphatism; (2) syphilis of the central nervous system; (3) cardiac disease, especially myocarditis; (4) aneurysm and arteriosclerosis; (5) severe pulmonary disease; (6) hepatic disease; (7) gastric and intestinal catarrh; (8) renal disease with blood casts and albumin; (9) alcoholism; (10) acute septic conditions; (11) a constitutional tendency to skin disease.

Danger signals during treatment are loss of weight, headache, insomnia, and loss of appetite, the onset of renal symptoms, stomatitis, diarrhoea, jaundice, and erythema. These symptoms are an indication for temporary suspension of treatment and caution in restarting. In the case of erythema, which may develop into severe dermatitis, an interval of from 1 to 6 months should elapse, according to the severity of the case. Bleeding to 18 or 20 oz., purging and large quantities of barley water are recommended for this condition. In the cases of convulsions with coma, bleeding to 18–20 oz., lumbar puncture with withdrawal of 15 c.c. of fluid, and intramuscular injection of $1\frac{1}{2}$ c.c. of a 1 in 1,000 solution of adrenalin are advised.

A Committee of German clinicians, neurologists, dermatologists, otologists, ophthalmologists, and pathologists has issued a report on salvarsan, based on information obtained from 182 German, Dutch, Austrian, and Danish doctors. The report, which is reviewed by Meirowsky, deals with 13,000 injections of old salvarsan, 40,954 of sodium salvarsan, 171,826 of neosalvarsan, and 64,500 of silver-salvarsan. Out of the total injections of old sodium, and neosalvarsan there were 12 deaths attributable to the drug (1 in 18,815); but as some of the fatalities might have been avoided by more careful precautions the chance of death is put at 1 in 56,445 (1 in 13,000 with old salvarsan, 1 in 20,000 with sodium salvarsan, 1 in 162,800 with neosalvarsan. Naturally, the dose played an important part in the mortality, especially with neosalvarsan. The mortality with this was 1 in 162,800 with doses not exceeding 0·6 grm., but if this was exceeded it rose to 1 in 3,000.

Encephalitis and dermatitis were found to be more liable to occur after an overdose. Hence the Committee recommend that larger doses of neosalvarsan than 0·6 grm. should not be supplied. Icterus occurred in about 1 in 2,000 injections of old salvarsan and sodium salvarsan; in about 1 in 6,000 with neosalvarsan. Early and late icterus were equally observed. Late icterus was found to be more frequent after large terminal doses and after a large total dosage. Dermatitis occurred in 48 cases, 5 of which were fatal; they appeared to have no relation to the preparation, dose, or method of administration. That the dermatitis was due to salvarsan and not to mercury was proved by its occurrence in 11 cases which had no mercurial treatment. In some cases the dermatitis recurred when salvarsan was repeated; in other cases it did not. Neuro-recurrences occurred in 15 cases: 1 with old salvarsan alone, 6 with sodium salvarsan and mercury, 4 with neosalvarsan and mercury, 4 with silver-salvarsan (1 with mercury). The Committee confirm the view that neuro-recurrences are due to insufficient dosage. Cerebral symptoms were noted in 6 cases (3 of primary and 3 of secondary syphilis) from 2 to 5 days after the last injection, and consisted in headache, loss of consciousness, vomiting, and convulsions. These symptoms, which only lasted a few days, resembled those of the fatal cases of encephalitis, and only differed in their mildness.

Toxic effects of neosalvarsan. Fildes and Parnell report on the toxic reactions following intravenous injections of neosalvarsan (neokharsivan and novarsenobillon). All the cases were otherwise healthy and most of them suffering from early syphilis, so that the results were due to the drug itself, and were not complicated by other infirmities. The number of men treated was 1,250, and the course consisted of six doses of 0·45 grm. given intravenously with two-day intervals. This report deals only with the toxic effects of the drug and does not include 'endotoxic' reactions, which are attributed to liberation of the syphilis toxin from the spirochaetes by the destructive action of the drug, and which is manifested by fever, headache, and nausea arising several hours after administration. Nor does it include the reaction caused by impurities in the water, which is manifested by fever, rigors, and sometimes severe general symptoms arising very soon after injection. According to McIntosh and Fildes, this reaction is due to protein derivatives from dead bacteria which were present in the water before sterilization, and can be avoided by sterilizing the water immediately after distillation and using it soon after the flask is opened.

Toxic effects occurred in 78 out of 6,588 injections, or a little over 1 per cent. only. They were most frequent after the third injection. When a toxic reaction occurs it does not necessarily indicate suspension of treatment, for it was found that continuation of treatment did not necessarily give rise to further symptoms of poisoning. It was found that there was a susceptibility to toxic reaction after the third and fourth doses, but less so after further doses. This observation does not support the view that the toxic reactions are due to an accumulation of arsenic.

The toxic effects observed included pyrexia 47 cases; skin eruptions 38 cases, erythematous, macular, papular, follicular, and polymorphic; headache 33 cases; suffusion of the eyes 26 cases; nausea and vomiting 17 cases; oedema 9 cases, general or limited to face or hands, and generally associated with erythema and other toxic symptoms; pains in various regions 9 cases; herpes 3 cases, usually of the upper lip; rigors 3 cases; delirium 2 cases; coryza 2 cases; jaundice 2 cases; albuminuria 2 cases. Other less frequent symptoms were dryness of the throat, air hunger, salivation, cyanosis, biliuria, tenderness over the gall-bladder, diarrhoea, sore throat, cutaneous hyperaesthesia. All of these were only observed in one instance.

The precautions advised by these investigators with a view to diminish the incidence of toxic reactions are simple. They include restriction of diet on the day of the first injection only (to avoid endotoxic reactions); rest in bed after injection till next morning; ambulatory treatment they consider more likely to be followed by toxic reactions. Abnormalities in the urine and old cases of visceral syphilis require caution in dosage. The technique they employed consisted in dissolving the full dose, 0·9 grm., in 10 c.c. of sterile distilled water, fractional doses being proportional. A 20 c.c. all glass syringe, with a three-way stop-cock, was used, by which saline solution could be injected immediately before and after the drug. The water used was from an ordinary still (glass stills being considered unnecessary), collected in hard-glass flasks, plugged with wool and autoclaved. After sterilization the flasks were covered with paper dust-caps and sealed. Water prepared in this way will keep indefinitely, but when once a flask has been opened it must be used immediately.

Silver-salvarsan. Boas and Kissmeyer have treated 62 cases of syphilis in every stage with silver-salvarsan, 400 tubes of which were sent them by Kolle for investigation. They note that most German investigators give silver-salvarsan without mercury, taking the risk of serious lesions of the nervous system. The authors are too sceptical as to the efficacy of the new remedy to dispense with mercury, and their results must therefore be judged accordingly. They found that the new preparation differed in no respect from the earlier drugs of the salvarsan group as to its action, but as this is as effective as that of old salvarsan, and as silver-salvarsan is much more soluble than old salvarsan, this preparation marks a definite advance, provided its effects prove as permanent as those of the old salvarsan.

Another Danish writer, Korsbjerg, shows much greater enthusiasm for silver-salvarsan, which he has tested at the Rudolph Bergh Hospital, Copenhagen, since July 1919. He and his chief, Jersild, were so impressed by its action in their first few cases, that they decided to dispense with mercury, intending to withhold it till the course of silver-salvarsan treatment was completed. Later, they were so impressed by the results achieved by silver-salvarsan alone, that they found it superfluous to follow up this treatment with a course of mercury. Of their 32 cases, 19 were already in the second stage, and, taken as a whole, they were serious, often neglected, cases. Yet in practically every case all the symptoms had vanished within a fortnight of the first injection. Of the 29 cases in which Wassermann's reaction was positive when the treatment was begun, 20 gave a negative reaction during treatment. Three patients, whose positive reaction persisted, had relapsed after earlier salvarsan treatment. Korsbjerg's enthusiasm for this new preparation does not, however, prevent his recommending the simultaneous administration of potassium iodide—a precaution reflecting not on his own experiences, which have been entirely satisfactory, but on reports from Germany of neuro-recurrences.

Further experience with silver-salvarsan shows that secondary effects appear to be more frequent than with neosalvarsan. Dreyfus, who has studied the causes of these effects, classifies them as follows: (1) Anaphylactoid symptom-complex, manifested by redness and swelling of the face and buccal mucous membrane. (2) Pyrexia, which may be due to liberation of endotoxins from dead spirochaetes after large doses or to chemical and bacteriological impurities in the water. (3) Cutaneous eruptions—urticaria and scarlatiniform eruptions which are generally transient, occasionally severe dermatitis. Dreyfus had only six cases of cutaneous eruptions in 1,000 injections, one of acute exfoliative dermatitis. 4. Syncope, collapse, vomiting, vertigo, and headache, occasionally occur. 5. Icterus has been reported. In most cases these secondary effects are mild, but Riecke reported a case of acute exfoliative dermatitis which was followed by broncho-pneumonia and death. Dreyfus considers that secondary effects after silver-salvarsan would be more frequent if this drug were in more general use, as it is more difficult to administer than neosalvarsan. However, he thinks they may be reduced to a minimum by commencing with small doses of 0·02 or 0·03 grm., and gradually increasing to 0·05, 0·075, 0·10, 0·20, and 0·25 at intervals of 3 days. If reaction occurs the injections should be stopped and begun again with a small dose. Morbilliform eruptions and erythema of the face are often premonitory signs of severe reactions and indicate cessation of treatment for 14 days, after which treatment should be continued with small doses at longer intervals, of 5 days. It is also advisable to use a dilute solution, of not more than 1 per cent.

Sinn reports five cases of **neuro-recurrence,** one after silver-salvarsan, three after old salvarsan, and one after neosalvarsan. In the case occurring after silver-salvarsan the facial and auditory nerves were affected one month after treatment for secondary syphilis. In the case occurring after neosalvarsan the facial nerve was affected two months after treatment for primary syphilis. In the cases occurring after old salvarsan the auditory nerve was affected in one five weeks after treatment; the oculo-motor and abducens nerves in another. The third case treated with old salvarsan was remarkable in that the changes were limited to the pupil, and consisted in inequality and sluggish reaction to light, reaction to accommodation being normal. The occurrence seven months after infection, and the negative Wassermann reaction in the blood and cerebrospinal fluid, in this case were against tabes.

With regard to the nature of 'neuro-recurrences' and their relation to salvarsan treatment, Klauder mentions cases in which the cerebrospinal fluid changed from negative to positive pleocytosis after salvarsan administration, and regards such changes, together with the provoked positive Wassermann reaction, as probably an expression of a Herxheimer reaction. He also regards the 'neuro-recurrence' as an expression of the same reaction. This phenomenon he divides into two stages, the laboratory or asymptomatic, and the clinical or symptomatic.

Concerning the alleged increase of neuro-recurrences since salvarsan was introduced, Klauder says that this is true in a sense, but is due to the improper and haphazard use of the drug. He condemns the exclusive treatment of syphilis with salvarsan, especially in the stage of acute general infection. The most rational treatment, he remarks, at this period is that which will minimize the possibility of the occurrence of a neuro-recurrence, namely, the thorough administration of mercury preceding salvarsan, and then the use of salvarsan in small doses for the first few injections, followed by its persistent administration in courses. The Herxheimer reaction he looks upon as of bad prognosis, and the neuro-recurrence as the bugbear of salvarsan treatment.

Three cases of **toxic jaundice,** one fatal, following intensive treatment with arsphenamin and mercury, are reported by Lynch and Hoge. All the patients were healthy men, and in all there was rapid onset of similar symptoms—jaundice, pain in right lumbar region, paroxysmal vomiting, delirium, and tenderness over the liver. There was an interval between the cessation of treatment (8, 10, and 11 intravenous injections of arsphenamin respectively, combined with mercurial inunction) and the onset of symptoms. In the fatal case, haemorrhages were found in the viscera and tubular nephritis, the liver was small and necrotic, but with little fatty degeneration. No arsenic was found in the liver nor in the urine. Lynch and Hoge remark that the negative tests for arsenic do not eliminate arsenic from the aetiology, and conclude that the condition was due to the toxic effect of arsenic on the liver combined with faulty elimination due to mercurial nephritis. They mention three similar cases, all fatal, reported by Fenwick, Sweet and Lowe, and Veale and Wedd.

Although it has been shown that intramuscular injection of arsenobenzol is, on the whole, as effective as intravenous, the former method has hitherto suffered from the disadvantage of causing local pain and swelling, sometimes so severe as to cause abandonment of this form of medication. Lévy-Bing and Gerbay claim to have surmounted this difficulty by employing an aqueous solution of the new arsenical compound **sulpharsenol.** The drug was dissolved in sterilized distilled water in the proportion of 0·06 grm. to 1 c.c. for doses not exceeding 0·24 grm.; for larger doses 0·12 grm. to 1 c.c. The initial dose was 0·06 grm., gradually increased to a maximum of 0·48 grm. The injections were given every two or three days, the number varying with the nature of the case and the tolerance of the patient. In the majority of cases there was no pain and no reaction, either early or late. Some patients, who had shown reactions, even ‘ nitritoid crises ’, with intravenous injection of sulpharsenol tolerated intramuscular injections without any trouble. The therapeutic results were almost equal to those obtained by intravenous injection. Lévy-Bing and Gerbay remark that the intramuscular administration of arsenical compounds is not only simpler and free from the unpleasant reactions and not infrequent dangerous effects of intravenous administration, but also more suitable for many syphilitic conditions. For example, while the intravenous route is indicated in urgent cases, and in the attempt to abort the disease, a patient with old or latent syphilis should not be exposed to its risks. For such cases the intramuscular route is preferable. They also point out that the dangers of intravenous injection are caused by too great rapidity in administration, a sudden rush of the drug into the bloodstream producing a shock and immediate intolerance, which is manifested by nitritoid crises, anaphylactoid disturbances, or by arsenical intoxication. This intolerance is avoided by the slower absorption of intramuscular injection. Even when the intravenous route is suitable for the first injection, they think that subsequent injections may, with advantage, be continued by the intramuscular method.

Patzschke recommends the local application of a **syrup of neosalvarsan** to primary sores, secondary lesions of the buccal cavity, condylomata, &c. The syrup consists of a 1 per cent. solution of neosalvarsan in 60 per cent. cane sugar. It is said to keep for a week, and has the advantages of rapidity in sterilization and absence of irritation.

Fildes and Parnell have investigated, at the R.N. Hospital, Haslar, the results of **arsenical treatment without mercury.** The course of treatment consisted in 6 intravenous injections of 0·45 grm. of neosalvarsan at intervals of 3 days. No mercury was given and none was advised afterwards, but in many cases mercury was given by others after the cases had passed out of their hands, thus vitiating the results. The cases were classified into four classes; class A included cases with chancre, but negative Wassermann reaction; class B included cases with chancre, adenitis, and a positive Wassermann reaction; class C included cases with signs of general infection and a positive Wassermann reaction up to 18 months from date of infection; class D included cases with no signs over 18 months from date of infection. Thus, classes A and B included all cases of primary syphilis, class C cases of recent secondary syphilis, and some early tertiary lesions, class D late secondary, tertiary, and latent infections.

In judging the results of treatment cases were recorded as 'failures' when clinical signs of relapse occurred; when the Wassermann reaction, after becoming negative, again became positive; when this reaction was not negative after four months' treatment. No cases were recorded as 'successes' because the authors admit that there is no criterion as to what constitutes a success. The records deal only with those men from whom specimens of blood were received after discharge from hospital; unfortunately, many were not heard of again. The results were as follows: In the A cases (pre-Wassermann primary) there were no failures; in the B cases 21 per cent. failed; in the C cases 23 per cent. failed; in the D cases 72 per cent failed. In the cases given mercurial treatment by other medical officers after discharge from hospital, contrary to the original plan, there was no evidence that this had any appreciable influence. With regard to lumbar puncture, Fildes and Parnell found no instance in which the cerebrospinal fluid showed changes when the serum reaction was negative and there were no other signs of active syphilis. They regard lumbar puncture as of value in prognosis, but of little value as a test of cure when other tests are negative.

Spittel considers **intravenous injections of mercurous iodide** the best method of mercurial medication to reinforce salvarsan. After experimenting with various preparations of arsenic, mercury, and iodide he found mercurous iodide the most effective. The formula is as follows:

Mercurous iodide	3·24 grm.
Sodium or potassium iodide	28·42 grm.
Phenolphthalein 0·5 per cent.	1 c.c.
Sodium hydrate	about 6 c.c.
Distilled water	1,000 c.c.

Before the addition of sodium hydrate the solution is acid. Phenolphthalein is used as a test for alkalinity and as a colouring agent. Sodium hydrate is added gradually till the pink colour shows alkalinity. The solution keeps well, but may become decolorized after a time owing to the formation of hydriodic acid. A few drops of sodium hydrate will restore alkalinity. The solution before injection is filtered through aseptic wool and diluted with an equal quantity of distilled water. The dose was 8 to 10 c.c. gradually increased to 12 c.c. The average number of injections was 5 to 6, given at intervals of 7 to 10 days, either alternately with salvarsan or in successive courses. The reaction was slight. The Wassermann reaction became permanently negative after such a course. Spittel states that the action of mercurous iodide given as above is much quicker than with other modes of administering mercury and iodide, and that one dose often acts as effectively as salvarsan. He advises continuance of treatment for a year by six-week courses of grey powder with intervals of a month, during the middle 10 days of which iodide of potassium is given.

Milian recommends intravenous injection of the **cyanide of mercury,** because it is the only salt of mercury which can be injected intravenously in concentrated solution without causing changes in the blood or vessels, and because of its great therapeutic activity, which he attributes to its high percentage of mercury (79 as compared with 73 of the perchloride) and also to the antiseptic power of the hydrocyanic acid. He used a 1 in 200 solution (in 90 per cent. saline) instead of the 1 in 100 formerly used. This solution can be sterilized without decomposition. The minimum dose is 1 cgm., the maximum 2 cgm. He thinks that daily doses are essential, up to 20 or 30. The intramuscular route may also be used. Cyanide of mercury is well tolerated by the kidneys, producing polyuria, and is indicated in syphilitic nephritis. Immediate reactions include cardiac distress and syncope and a febrile Herxheimer reaction; later reactions, stomatitis, diarrhoea, vomiting, and colic. These reactions are less liable to occur with the 1 in 200 solution, injected slowly, and given before meals, and when glycerophosphate of lime is given daily in 1 grm. doses. When toxic symptoms do occur the injections should be omitted for two or three days, and then diminished in dose or given on alternate days.

Treatment of neurosyphilis. Van der Valk points out that changes in the cerebrospinal fluid may persist after the blood has become negative after treatment, so that the patient cannot be considered cured. Nor can a case of primary syphilis be considered cured, even if the cerebrospinal fluid is negative after energetic treatment, for a neuro-recurrence caused by spirochaetes which have remained in the central nervous system may develop later, with recurrence of changes in the cerebrospinal fluid. Hence, to claim an abortive cure without control of the cerebrospinal fluid is unjustifiable. Van der Valk recommends that the patient should have a lumbar puncture two months after cessation of treatment, another two months after this, and then every six months for three years; but, as he remarks, few patients will submit to this, so that abortive cures must be rarely proven.

Concerning the method of treatment, Van der Valk advises a preliminary course of mercury for a few days before commencing salvarsan, as this diminishes the liability to neuro-recurrences, and also the danger of a cerebral Herxheimer reaction, which he holds to be the cause of haemorrhagic encephalitis. He also recommends that the first two doses of salvarsan should be small ones and given with a week's interval. If these are well borne the dose should be increased.

In conclusion, Van der Valk sounds a note of warning against the so-called abortive cure of syphilis, and points out that a sufficient number of years has not yet elapsed to tell whether such 'cures' will be free from tabes and paralytic dementia. Indeed, as he remarks, it is quite possible that there will be in the future an increase in these affections directly due to this 'abortive' treatment.

Kolmer describes a **new method of treatment for neurosyphilis** which he considers an improvement on the Swift-Ellis and Ogilvie methods. This method is as follows: (1) A course of treatment lasts four weeks, during which period 24 inunctions of mercury, 360 grains of iodide of potassium, and four combined intravenous and intraspinal injections of arsphenamin are given. Treatment is begun with daily inunctions of mercury and 5 grains of iodide three times a day for a week. After this four weekly intravenous and intraspinous injections of arsphenamin are given. The inunction and iodide are continued except on the days of injection. The urine is examined once a week for signs of renal irritation. The patient is kept in bed and given a light diet on the days of injection.

(2) The dose of arsphenamin is 0·6 grm., dissolved in 150 c.c. of sterile saline solution, and rendered slightly alkaline by 15 per cent. sodium hydrate solution. Sterile saline solution is added up to 200 c.c. Each c.c. of the solution now contains 0·003 grm. of arsphenamin; 1 c.c. of this is removed to a sterile test-tube, to be used later in doses of 0·1 c.c. (0·0003 grm.) for adding to serum *in vitro*.

(3) Immediately after intravenous injections 25 c.c. of blood are removed from the opposite arm and added to a 50 c.c. sterile centrifuge tube containing 4 c.c. of 10 per cent. sodium citrate solution, to prevent coagulation of blood. The mixture is centrifuged for 20 minutes, and 10–12 c.c. of serum is pipetted into a sterile test-tube. To this is added the dose of arsphenamin, already prepared (0·1 c.c., or 0·0003 grm.), to make arsphenamized serum.

(4) Lumbar puncture is now performed, and about 30 c.c. of spinal fluid allowed to escape; 10 to 12 c.c. of the arsphenamized serum is then slowly injected, by gravity or by syringe. The spinal fluid removed is kept for examination. The patient remains in bed, with the foot of the bed elevated, till the next day. The time required for the operation is about two hours. The advantages claimed for this method are:

(1) Combined intravenous and intraspinal treatment.

(2) Blood is removed at once instead of after an interval of an hour, and thus contains more arsphenamin.

(3) Treatment is completed at one sitting.

(4) The removal of 20 to 30 c.c. of cerebrospinal fluid, followed by the injection of only 10 to 12 c.c. of arsphenamized serum, probably leaves the pressure reduced for some time, producing increased vascularity and transudation, with the beneficial results ascribed above to spinal drainage.

(5) The patient receives the benefit of treatment with mercury and iodides, and of spinal drainage while under the influence of these antisyphilitic remedies.

The only contra-indication to the method is the occurrence of a reaction following the intravenous injection of arsphenamin. In such an event a second specimen of blood may be obtained after the reaction is over, and used next day.

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DISEASES OF THE SKIN

There has been a considerable increase in the output of papers bearing on diseases of the skin since the armistice. During the period of active hostilities, dermatology (with the exception perhaps of its venereal aspects) was rather overshadowed by matters of more immediate military importance. There is, however, no great advance to record either in pathology or therapeutics. A large part of the papers are devoted to recording interesting and unusual cases and to speculations thereon. Of late there has been an increasing tendency to invoke the **endocrine glands** to explain dermatological phenomena of various kinds. In some cases it is thought that there is an excessive secretion of the active hormones; in others, and perhaps more often, that there is a deficiency. This subject is discussed fully by Nobl. He includes among dermatoses due to endocrine disturbances acne which he correlates with activity of the sexual organs, a large group of menstrual rashes including herpes progenitalis, while he points out that many dermatoses become much worse at the menstrual period. The severe form of alopecia areata, which occurs in syphilitics but which is not exactly a manifestation of the disease, he suggests may be due to a syphilitic disturbance of the internal secretions. Impetigo herpetiformis is correlated with the hormones of pregnancy, ichthyosis is well known to be associated with hypothyroidism. Hypertrophy of the pituitary body causes the growth of hair in unusual situations, while hypopituitarism is associated with poorness of hair and dystrophia adiposo-genitalis and also with dermatographia. He says that the skin affections due to the thymus are doubtful, but he thinks that it may be associated with urticaria and chronic seborrhoeic eczema. Pigmentation due to disease of the suprarenals is well known. He mentions an interesting case under his own care in which the patient had, in addition to the ordinary pigmentation, arsenical hyperkeratosis and a papular itching eruption. Nobl cannot say that the results of treatment by administration of suprarenal products has often been satisfactory. Roesch, again, is inclined to think that sclerodermia is caused by a disturbance of not one alone, but of several of the endocrine glands. He had a case associated with very low blood-pressure, areas of dark pigmentation, and emaciation which suggested that both the thyroid and suprarenals were involved; she benefited to a certain extent both by thyroidein and adrenalin. A case somewhat similar of concretions of chalk under the skin is published by Drucker; this also is possibly of the same nature. Atwater also publishes a case of sclerodermy and sclerodactyly, but he obtained no benefit from the exhibition of thyroid.

The *British Journal of Dermatology* devoted one number in 1919 to a symposium by some of the leading British dermatologists on **vaccine therapy** in diseases of the skin. Papers were contributed by Adamson (1), Whitfield, Sequeira and Western, and Macleod and Topley. Considering the extensive and popular use of vaccines in dermatology, the opinion of these writers of their value is distinctly disquieting. Adamson is frankly pessimistic about them, the only type of case in which he admits that they are of any use at all is a recent outbreak of furunculosis. He concedes that very occasionally strikingly good results do occur as the result of vaccine treatment, but deplores the fact that we have no precise means of knowing in what doses to employ it and no sound explanation for its action. 'Nor do we know why in the majority of cases it fails to effect a cure and only occasionally gives satisfactory results.' The other writers are only slightly more optimistic; all agree that chronic staphylococcic sycosis is extremely refractory to vaccines, and that tuberculin in lupus, although occasionally it gives temporary improvement, never confers lasting benefit, also that the comedo stage of acne is unaffected by vaccine treatment and that the pustular sequelae are very seldom ameliorated. Whitfield finds that in certain diseases which usually run a short course under ordinary treatment vaccine treatment often achieves brilliant results in the exceptional cases where the disease proves resistant and threatens to degenerate into a chronic malady (e. g. streptococcic impetigo in delicate children or contracted under active service conditions). He has also obtained good results in cases of eczema occurring in patients the subjects of intestinal dyspepsia. Such cases he treats with vaccines from their own faeces. Sequeira mentions that he has obtained healing of a refractory carbuncle by *Staphylococcus aureus* vaccine after repeated surgical operations had failed, good results in erysipelas from a suitable streptococcus vaccine, also occasionally in ulcers from mixed infections, and in that rare condition gonorrhoeal keratodermia. Macleod has obtained satisfactory results in boils alone, otherwise he is profoundly dissatisfied with vaccine therapy. On the other hand, Barber (1) thinks more highly of these methods; he publishes a case of lupus erythematosus cured by a streptococcal vaccine obtained from the tonsil, but in addition to vaccines the complete surgical removal of all infected lymphoid tissue was carried out. He also publishes, in association with Knott, a very interesting case of recurrent ulceration apparently due to a diphtheroid bacillus in which he got good results from a vaccine made from the diphtheroid organism. Chary as one must be of accepting a diphtheroid as the cause of a disease, his account of the way the bacteriology of the case was worked out is very convincing.

The traces of war are still discernible in dermatological publications. Wassermann has a paper of some length on the pathogenesis of **septic dermatoses** in war time. He ultimately arrives at the conclusion, suggested indeed by common sense, that bacterial infection, although present, plays a less conspicuous part in the causation of these conditions than a toxic state induced by disturbed metabolism—in modern phraseology, disorders of the normal hormones. This disturbance is shown by alterations of the blood-count, consisting chiefly in the presence of mast-cells and the lack of eosinophils. He concludes that these pyodermatoses must therefore be placed among the group of *deficiency diseases*.

Another result of the war has been a widespread epidemic of **ringworm** throughout Central Europe. A good many papers have been written about it. Nobl says that ringworm of the beard has become increasingly common in Vienna. New species of trichophyta, previously unknown or at least rare, have made their appearance. Formerly the *Trichophyton cerebriforme* of the neoendothrix group was the prevailing type, but more recently the *T. gypseum* has become much more common. This causes both superficial and deep lesions, sometimes side by side. It is probable that in passing from man to man it loses its original characters and thus becomes capable of causing superficial lesions. The origin of the epidemic is no doubt in men returning from the army who have been brought much into contact with animals, hence the animal ringworms. The channel of propagation is no doubt mainly by the barber's shops. This explains the fact that the epidemic is almost confined to men. Were the infection spread by means of towels, &c., women would be more often attacked. Careful observation is necessary to avoid the error of mistaking it for eczema or pityriasis alba. The treatment is by no means easy, and the disease usually lasts several months. Apparent cure is often followed by relapse. The patients are encouraged to shave under proper precautions and to use a 1 per cent. or 2 per cent. solution of salicylic acid or resorcin in alcohol. Infiltrated nodules are epilated with forceps. The author warns us that epilation by X-rays, like other treatments, is often followed by relapse unless the infiltrated nodules are specially treated and sterilized. Almost all observers agree in finding that the treatment of beard ringworm is far from easy. Several have attempted to use various means for increasing the general resistance of the patient either by the injection of turpentine oil or of one of the vaccines derived from cultures of ringworm. These are supplied commercially under the name of *trichophytin* or *trichon*. Löwenfeld and Pulay have also tried several other different bodies as antigens, such as albumose-free tuberculin, new tuberculin, and old tuberculin. They were not much impressed with the results obtained, but found that on the whole better results were got from the use of specific antigens (i. e. trichophytin and its variations) than from non-specific. Fischl has got good results in deep-seated infections from the use of trichophytin combined with the use of strong resorcin paste. A definite reaction follows the injection of trichophytin both general and local; this sensitiveness remains long after the attack of ringworm has been cured. The only optimist about the treatment of ringworm of the beard is Wetterer, who pins his faith to the 2 per cent. ointment of trypaflavin. In cases of folliculitis he uses very hard X-rays and disapproves the use of moist applications. Löwenfeld has a very practical paper on the best methods for preventing infection in the barbers' shops. He experimented with various methods of disinfection, trying them both on cultures of the fungi most commonly met with, and also upon hairs and scales taken from infected persons. He placed small particles of the cultures, or scales, or hairs in the disinfecting fluid to be tested, for periods varying from five to thirty minutes and then planted them out on maltose agar. He found that five minutes' immersion in boiling water was always sufficient to prevent growth. Alcohol of 80 per cent. he found inhibited a culture after ten minutes generally, after half an hour always, but on the other hand a hair immersed in it for half an hour was still capable of giving rise to active growth. Formalin 2 per cent. solution was somewhat more satisfactory, for ten minutes' immersion in this liquid always killed a culture and almost always sterilized hairs. Carbolic acid in practicable strengths and oxycyanide of mercury in 1 per cent. solution he found almost useless. On the other hand, a 10 per cent. soda solution was always effective in five minutes at 80° C. In fact this and boiling water he found to be the only reliable disinfectants. These, however, are hardly practical owing to the damage which they do to the barbers' instruments, and finally he was driven to the conclusion that the chief reliance must be placed upon mechanical disinfection, in other words, scrupulous cleanliness.

Klehmet describes a remarkable epidemic of small-spored ringworm of the scalp occurring in an orphanage in Hanover. About 20 out of 200 children were affected. The remarkable point was the refractory behaviour of the disease to X-rays. Not only did the hair upon the infected areas fail to fall out with the same dose which caused defluvium of the healthy hair but the hair papillae were apparently stimulated even to more vigorous growth. X-rays were only effective when they were preceded by the use of unusually strong antiseptic applications and hot poultices. Cultures were made of the fungus and were submitted for identification to Professor Plaut, who pronounced them to be in all probability *Microsporon pertenue*, a species up to that time unknown in Germany. Another case of rare fungoid infection is published by Engman and Weiss, who describe a case of infection of the mouth by *Monilia candida*.

Papers of general dermatological interest, but somewhat off the usual lines, are one by Varney on **deranged sebaceous secretion** as a factor in diseases of the skin, and by Scholtz on **dermatologic misnomers.** Varney considers that lack of sebaceous secretion is a far more common deviation from the normal than the excess which acts only during adolescence, and is the cause of seborrhoea and acne. Lack of sebaceous secretion causes the skin to look sallow and non-transparent. He thinks that much harm is done by a too frequent employment of soap and water, especially in winter. The result is a hard dry skin which often cracks, with a consequent liability to infection, and is often associated with a sub-normal temperature.

Scholtz is a literary purist and has many objections to put forward against current dermatological nomenclature. His paper hardly admits of abstraction, but perhaps it may be said that any attempt to reform our nomenclature needs to be very carefully undertaken lest the confusion, of which he, with much justice, complains, be even worse confounded.

As always, many interesting cases have been published by many observers, which hardly yield to any formal classification.

Graham Little has collected his ripe experiences of **lichen planus**; they are interesting statistically, but they do not disclose anything very new on the subject. Adamson publishes three cases of lichen planus in children of very tender years, the youngest only two years old. This is remarkable, for lichen has always been regarded as almost exclusively affecting adults.

Sabouraud writes pessimistically on the internal treatment of **psoriasis.** He emphasizes the incurability of the disease, although he admits that there are mild cases which appear to be cured because the intervals between the attacks are very prolonged. He has no faith in the dietary regulation of psoriasis, merely conceding that undue indulgence in alcohol has a prejudicial effect upon it. Of the various drugs which have been tried in the internal treatment he mentions as useful cacodylate of soda and enesol. He himself has used enesol in a large number of cases over a period of ten years with improvement in about half the cases, at all events for a time. He also speaks well of X-rays. Recently Danysz has had good results from vaccines prepared from the aerobic bacteria found in the large intestine. Sabouraud has also obtained good results in some instances by this means. The only common factor in the various internal treatments of the disease is the shock (*secousse*) which they give to the organism, using the word 'shock' in a very loose sense. Up to the present there is no specific treatment, but we may hope for better results from persistent and patient research.

Bory writes strongly in favour of the parasitic origin of psoriasis. He supports the theory on several grounds:

(1) The frequency with which the disease begins in a wound or scar.

(2) The occurrence of the disease in families. He explains this undoubted fact by contagion, ignoring the influence of heredity, which previously has been supposed to explain it.

(3) The spread of the disease he explains by a series of autoinoculations from one patch to the next.

The three following conditions he postulates as necessary for the outbreak of the disease:

(1) A break (*effraction*) more or less complete of the integument.

(2) A special sensitiveness of the organism, at all events at the site of inoculation.

(3) The proximity of the unknown infective agent.

He thinks he has found in the deeper layers of the psoriasis patches traces of mycelial growth something like *Microsporon minutissimum*, perhaps an oospore. He has not been able to cultivate it.

Barker and Carter describe a case of **pemphigus vegetans** remarkable for its long duration. It began after digestive disturbances followed by an eruption described as 'urticarial'. The lesions were typical and affected the lips, palate, pharynx, and genitalia. They presented elevated edges consisting of closely-set vesicles containing turbid fluid. The patient, a young woman, was greatly emaciated. From time to time she had very considerable remissions of her symptoms. A complete pathological study threw no light on the origin of the condition. As so often happens in these cases, she was treated energetically for some time on antisyphilitic lines with a total absence of success.

Rutherford describes an epidemic of **alopecia** which he observed in France during the advance of 1918 over the territory which had been long occupied by the Germans. He found that a very large proportion of the inhabitants were afflicted by falling of the hair. He ascribed this to their past dangers and privations. In most cases there was a general defluvium, but in a few the alopecia was of the areata type.

The relationship between solar keratoses and cancer is discussed by McCoy, who calls attention to the much greater frequency of cutaneous cancer upon those parts of the skin which are exposed to light than upon others. Like many other dermatologists, he believes that insolation produces keratoses and that these are the most common precancerous lesions. Blonde individuals develop keratoses more frequently than those of dark complexion, who quickly become tanned and thereby protected. Sunburn is produced not only by the direct rays of the sun but also by reflected light, whether from snow, water, or white buildings. Influence of occupation in causing keratoses is shown by the fact that 93·5 per cent. of his patients were farmers or their wives, or other persons engaged in outdoor occupations. None of the dark-skinned races are apparently liable to keratoses at all. On the other hand, the albino acquires no pigment under insolation, always suffers from solar dermatitis, and never becomes immune to the sun. Greater protection against the sun is advised for those who live open-air lives.

Saphier and Seyderheim describe a case of **chronic myeloid infiltration of the skin** in chronic myeloid leukaemia. There was no doubt of the diagnosis, for a large proportion of the white cells in the blood were myeloblasts. This is an example of an extremely rare condition, for most cases of leukaemic infiltration of the skin hitherto recorded have been lymphatic leukaemia.

Salomon discusses the biochemistry of **xanthoma** and **xanthaemia.** He finds that the colour is due to a lipochrome derived from lutein, which can be extracted from the serum by shaking it with ether. No xanthosis is possible without xanthaemia, but the converse is not true.

Skinner has studied a case of **multiple pigmented idiopathic sarcoma.** Like previous observers, he found no evidence of sarcoma, but he regards the disease as a reaction of all the dermal tissues to some chronic inflammatory agent, possibly a circulating toxin. This disease is possibly in some way related to Schamberg's disease, a study of which, based on five cases of his own, is published by Adamson (3), who discusses its relationships with varicose pigmentation and angioma serpiginosum.

Ulcerating granuloma of the pudenda is the subject of two papers by Driscoll and Goodman. Both agree that it is a most refractory condition.

Ward publishes a most extraordinary large **ulcer of the leg caused by bromides.**

Cockayne points out that acute **striae atrophicae** not infrequently follow influenzal pneumonia.

Smith publishes a case of what he terms an extensive **papulo-necrotic tuberculide.** His description and the photograph given, however, suggest rather a bad case of acne vulgaris, and it must be admitted that one's suspicions are deepened by reading that the eruption on the back and chest cleared up completely under a weak sulphur ointment, those on the forehead and temples less so.

Treatment. Yet another local treatment for lupus erythematosus is brought out by Small, who recommends rubbing the patches with a glass rod dipped in a mixture of pure carbolic acid one part and lactic acid fort. four parts. Needless to say, he claims excellent results.

In his lectures on treatment for the use of practitioners, Max Joseph calls attention to the fact that, although patients suffering from lichen planus often scratch themselves very severely, they never, unlike patients with lichen simplex chronicus, infect themselves with secondary septic diseases. Gerson has tested Bessunger's treatment of lupus vulgaris, which consists in combining the administration of large doses of iodine with Roentgen ray local treatment, the idea being to set free iodine in the tissues. She does not think that this method is to be recommended in preference to older and more convenient procedures. Ravaut writes recommending the use of cacodylate of soda and hyposulphite of soda, intravenously injected, for many obstinate dermatoses.

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H. D.

VINCENT'S DISEASE

Epidemiology. While Stuhl, of Giessen, regards Vincent's angina as very rare, having seen only three cases in twenty years, Bierotte, Director of the Municipal Bacteriological Laboratory at Münster, maintains that it occurs much more frequently than is generally supposed. The comparative rarity of the diagnosis he attributes to the fact that in a large number of cases no bacteriological examination is made. Having made it a practice to examine all throat swabs for the fusiform bacillus and spirillum, he found that among 216 swabs sent to him in 1919, 20, or 9·6 per cent., contained these organisms.

Several other German writers, such as Schoetz, Seligmann, and Finder of Berlin, and Kronenberg, of Solingen, draw attention to the recent prevalence of Vincent's angina in Germany. Thus Schoetz states that whereas between 1908 and 1918, he had met with only one case of Vincent's angina to every thirteen cases of ordinary tonsillitis, between September and October 1919 he had seen nine cases of Vincent's angina as compared with 33 cases of tonsillitis. Some of the patients had attributed their complaint to English cigarettes, but the erroneousness of this assumption was proved by the disease being equally prevalent among non-smokers.

According to David and Hecquet, of Galatz, an outbreak of bucco-pharyngeal ulceration occurred in the Roumanian army in the summer of 1918. It was at first mistaken for scurvy, which had been prevalent in the Roumanian army and civilian population at the end of 1917 and beginning of 1918, but subsequently the lesions were found to be due to the symbiosis of the fusiform bacillus and spirillum of Vincent. Generally speaking, the appearance of the lesions was associated with an inadequate food supply, though this was better than during the period of scurvy, and subsequently an outbreak of Vincent's angina occurred among several French units in Roumania in men who were all in good health and well-nourished. The local condition of the mouth did not furnish an explanation of the disease, for though some of the patients had bad teeth, in others the dentition was perfect.

Symptomatology. A case of Vincent's angina simulating chancre of the tonsil is reported by Cornaz. The patient, a man aged 26, developed an ulcer, the size of a five-franc piece, on the inner side of the right cheek. The floor of the ulcer was sanious, its base infiltrated, and the corresponding submaxillary glands were enlarged and tender. The temperature was normal. The ulcer cleared up under applications of tincture of iodine and hydrogen peroxide gargles in nine days' time. A fortnight later the patient developed a similar ulcer on the right tonsil. On admission to hospital eleven days afterwards the tonsil was red, infiltrated, and showed an ulcer the size of a franc covered with a diphtheroid deposit. There was a large, hard, and almost painless enlargement of the submaxillary glands. The left tonsil was normal. Temperature 97·8. The appearance of the lesion and its unilateral position at first suggested tonsillar chancre, especially as the patient admitted an abnormal sexual intercourse which had taken place six weeks previously. No *Spirochaeta pallida*, however, was found and the Wassermann reaction was negative. Vincent's organisms were found in a smear, and rapid recovery took place after local application and intravenous injection of novarsenobenzol.

Owing to the rarity of death from Vincent's angina the case reported by Young is of interest. The patient was a negress, aged 42, in whom the disease involved the floor of the mouth, the right side of the palate, the entire surface of the right cheek, the anterior and posterior pillars and tonsils, and part of the posterior pharyngeal wall. Free haemorrhage occurred, and, in spite of intravenous injection of salvarsan, death took place on the eighth day from secondary anaemia.

A case is also reported by Siebenmann of an ulcer at the root of the tongue due to the fuso-spirillar symbiosis in which rapid extension took place in spite of treatment and gave rise to fatal haemorrhage. It is doubtful, however, as Finder remarks, whether such cases should be regarded as Vincent's angina and not rather as a form of noma.

Involvement of the larynx by the fuso-spirillar symbiosis is a rare event. In 139 cases of Vincent's angina Reiche found the larynx affected in only one instance, and at the same time as the tonsil. Arrowsmith has reported a case of fuso-spirillar laryngitis without any angina. Du Castel and Dufour, from whose paper this information has been obtained, record a case in a soldier aged 20, who developed a violent attack of dyspnoea preceded by headache, pain in the back and limbs, and fever. Examination of the throat showed characteristic ulceration of the left tonsil, and on laryngoscopy an ulcer was seen on the middle of the free border and upper half of the epiglottis, smears from which showed fusiform bacilli and spirilla. Rapid recovery followed application of methylene blue.

Euler, of Erlangen, regards pyorrhoea alveolaris as a local spirochaetosis in which a special form of spirochaete, the *Spirochaeta pyorrhoica*, in association with the fusiform bacillus, plays an important part. Both micro-organisms may occur in a saprophytic form in normal gums, but are not pathogenic as long as they are present in only a normal amount. The disease is probably caused by a great increase in their numbers which is the result of a marginal gingivitis caused by local factors, especially tartar.

Bond, Professor of Genito-urinary Diseases in the University of Arkansas, states that several cases have been reported of *Vincent's infection of the penis*, which he regards as identical with what has recently been described as erosive balanitis, gangrenous balanitis, and, by Cabot, of Boston, as the fourth venereal disease. The predisposing causes are a long prepuce and lack of cleanliness, which allow the secretions to accumulate and render the mucous membrane a favourite culture medium for the bacillus and spirillum. The method of inoculation may be direct (oral coitus), or indirect (wetting the penis or labia with saliva from an infected mouth). After an incubation period of from three to five days the lesions usually begin on the glans as slight erosions with little or no induration. The edges of the ulcers are irregular, later becoming undercut and ragged. The bottoms slough and become covered with easily detachable greyish purple membranes. The secretion is dirty-greyish and the odour foetid. The prepuce becomes oedematous, usually causing phimosis. The inguinal glands are involved in exceptional cases. There may be lymphangitis. Although there is sometimes some malaise and the temperature may rise to 101° or 102°, there are usually no other general symptoms. Local applications of hydrogen peroxide are usually sufficient. Occasionally good results are obtained by touching the ulcer with tincture of iodine.

The corresponding condition in women which is known as *erosive or gangrenous vulvitis* is discussed by Driscoll, of Richmond, Virginia, who states that the predisposing causes are filth and prostitution. He reports three cases in all of which the genitals were extremely dirty and presented a large amount of discharge, so that ideal conditions existed for the growth of the fusiform bacillus and spirillum. In each case there was extensive ulceration, amounting in one instance to an almost complete destruction of the vulva. The inguinal glands were enlarged in all cases, but there were no signs of suppuration; all showed a slight degree of toxaemia. The Wassermann reaction was negative in all. There was no response to anti-syphilitic treatment including arsphenamin.

Treatment. Cahier points out that the aetiological, anatomical, and clinical identity of ulcerative stomatitis, mercurial stomatitis, and Vincent's angina justifies the employment of the same treatment in each of these affections. Although in simple and mild cases the ulcerative lesions may be cured by a variety of topical applications, in obstinate cases *arsenical products* alone have a constant success. Treatment by arsenobenzol may be carried out either by local application or, in exceptional cases, by intravenous injections or both processes combined. In stomatitis 0·10 to 0·30 grm. arsenobenzol in suspension in 5 to 10 c.c. glycerine is applied for ten to fifteen minutes once or twice daily after removing the tartar from the teeth. When the local and general signs are well marked or particularly severe, one or two intravenous injections of arsenobenzol a week in doses of

0·10 to 0·30 grm. should be given. Two or three injections are usually sufficient. Sebenq recommends daily gargling with a solution of arsenobenzol to cause the disappearance of the spirilla and fusiform bacilli and to prevent relapses.

As the ordinary local treatment of Vincent's angina requires a considerable time to be effective, Zemann recommends making a local injection of the floor of the ulcer with a 3 per cent. solution of neosalvarsan in sterile distilled water. Much more rapid results are obtained by this means without any bad local or general effects, a feeling of tension in the tonsil for one or two hours after the injection being the only complaint.

Capitan has treated 200 cases of Vincent's angina in soldiers by intragluteal injections of colloidal arsenic. As soon as the diagnosis was made by bacteriological examination, 6 c.c. were given. Local treatment was not considered absolutely necessary, but gargling with boracic lotion or peroxide might be used. A remarkable improvement took place in 24 hours, and in three or four days the ulceration was completely cured. In exceptional cases in which the fusiform bacilli and spirilla persisted, a second injection of 6 c.c. of colloidal arsenic was given 48 hours after the first, and within 24 hours the organisms disappeared. In a few cases in which other organisms persisted, two or three more injections of 3 to 4 c.c. were given.

According to Euler salvarsan has a very prompt effect on pyorrhoea alveolaris, producing at first a violent reaction followed by rapid diminution of the spirochaetes and improvement of the condition. In mild cases the local application of 10 per cent. salvarsan in vaseline or glycerine is sufficient, in moderate cases local injection is indicated, and in severe cases intravenous injections of salvarsan are required.

Barth, of the Leipzig University Clinique for diseases of the ear, nose, and throat, recommends the local application of *salicylic acid* as cheaper and less toxic than salvarsan or neosalvarsan. He uses a 10 per cent. solution in equal parts of alcohol and glycerine, the ulcer and neighbouring parts being rubbed with a swab dipped in the solution. Usually considerable improvement occurs within twenty-four hours. In addition he prescribes gargling every half-hour with a 10 per cent. solution of salicylic acid in alcohol, 15 or 20 drops being added to a glass of water.

The local application of a saturated solution of *chromic acid* on a swab is recommended for Vincent's angina and allied disorders by Dubreuilh, of Bordeaux, who has found arsenobenzol, locally and intravenously, and methylene blue unsatisfactory. After the application the patient is made to gargle so as to prevent him swallowing the chromic acid in his saliva, and gargling with hydrogen peroxide should be repeated several times during the day. The pain caused by the application is only moderate and is less than that due to other caustics. As a rule the ulcer is clean the next day, and it is only rarely necessary to make a second application towards the fourth or fifth day.

Lafite-Dupont and Lagarde report rapid improvement in Vincent's angina following irrigation and gargling with *Dakin's fluid*, the irrigations being performed with 1 part of Dakin's fluid to 3 parts of warm water twice daily and the gargling carried out several times with the same fluid in the intervals.

The intravenous, or, where this is impossible, the intramuscular injection of a 40 per cent. sterile solution of *urotropin* is recommended by Sachs, of Vienna, for Vincent's angina and stomatitis. The first dose consists of

10 c.c., the second dose on the next day is 15 c.c. or 6 grm., which in another two days is increased to 8 grm. and later to 10 grm. The number of injections required in Sach's cases ranged from one to eight. The disadvantage of local treatment is that it does not reach the causal organisms which are hidden away in the crypts and lacunae of the tonsil, whereas the formaldehyde excreted in the tissues after intravenous injection of urotropin either kills them or diminishes their virulence. The rapid cure of the angina effected by this method prevents the occurrence of complications.

Stuhl reports a case of Vincent's angina, in which, after failure of other methods, rapid recovery followed injection of Rosenbach's *tuberculin*, 1·82 c.c. of which was given in four injections.

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J. D. R.

THE TREATMENT OF VARICOSE VEINS OF THE LEG

An important number of the men called up for military service were found unfit owing to the varicose condition of the veins of the leg. Some of them had neglected treatment and the varicosities had in consequence become aggravated. Others had pursued until then their avocations without experiencing disability. In another group were men who developed varicose veins in the legs during military training, although whilst training they were leading generally a more healthy life than before, one in which there was more and better regulated muscular exercise and less of standing and sitting. The question is not a novel one, for the development of varicose veins has been noted in athletes, e.g. after running, the heart being quite strong. Hasebroek explained that under such circumstances an increased arterial pulsation is transmitted reflexly to the veins corresponding with the arteries, causing an increase in the natural rhythmic contractility of the venous wall, which in consequence undergoes an *active* hypertrophy. Granted a latent tendency to varicosity in the superficial veins, then two suggestions have been made. The muscular contractions drive more blood out from the deep veins through the anastomosing venules into the superficial veins. Alternatively muscular contraction may check the venous flow momentarily and so send a reflex impulse, like the sudden turning off of a water-tap which causes a vibration in the pipe. On active service, especially, owing to the long standing in the trenches, slight dilatation of veins caused the legs to become painful; this became a marked cause of invaliding. There was in consequence a call for operative treatment which did not entail a long stay in hospital and which allowed of the man returning quickly to the front. Moreover, as a consequence of injury to the lower limbs, including fracture, a varicosity may develop complicated to a variable extent by elephantiasis. Ulceration once started on the leg is liable to recur; the Wassermann reaction is an aid in distinguishing the ulcers especially due to syphilis; when the ulcer tends to be complicated by elephantiasis, the circular and spiral incisions and the excision of strips of fascia may perhaps be a means of preventing the stage being reached when amputation is the only means of affording relief.

Trendelenburg's method of examination is important but is not exclusive. The superficial veins are emptied by elevating the leg whilst the patient is lying on the back. Then pressure is applied over the saphenous opening and the patient stands up. On relaxing the compression, if the saphena vein suddenly fills, a loss of the function of the valves in the vein is demonstrated.

Stadel added three other signs of incompetence of the valves of the saphena vein, even although the examination following Trendelenburg has a negative result. Perthes in 1895 made the following observations: the patient stands up until the veins are full and then pressure, e.g., by a pad and bandage, is applied over the saphenous opening. He next walks about, when, if the valves are incompetent, the veins will become less distended, owing to blood being sucked into the deep veins. Hesse in 1913 first marked out the saphena vein on the inner side of the knee, over this the fingers are applied or a stethoscope, whilst the Trendelenburg test is being carried out. On relaxing the pressure over the saphenous opening, and a whirr being felt or heard, it will be evident that the valves in the vein above are no longer efficient. Then, also a cough impulse normally limited to the vein at the saphenous opening may be felt down the course of the vein as low as the knee.

In such cases, whatever else is done, the closure of the internal saphena vein close to its termination is generally indicated. The original proposal of Trendelenburg was merely to apply a ligature; this is not enough. The current soon re-establishes itself around and through the point. It is necessary to excise a length of the vein in order to prevent this. Also there are tributaries which join the internal saphena close to its termination; moreover the vein is frequently duplicated. The only satisfactory method is to excise some three inches, the upper ligature being applied at the saphenous opening so that the convergence of veins to this point can be cut off. A principal cause of recurrence after the above is the free communication between the internal saphena vein below the knee and the external saphena, which causes the patient to complain in particular of pain in the calf. Note should be taken of this communication when examining the patient whilst he is standing. To meet this an incision is made over the upper part of the internal head of the gastrocnemius parallel to its fibres, when, by retracting the margins of the wound, lengths of the internal and external saphena can be excised along with the communicating veins. The upper part of the incision must not encroach upon the internal condyle, nor the lower end be continued over the tibia. The merits of combining the two incisions is that the tendency to increase and to develop complications is arrested, and there is a radical cure in early cases. The objections raised against the procedure are that the conditions necessary for an aseptic operation are essential, also the patient must be kept in bed for 10 days or more. Alternative measures come under two headings: (1) Methods aiming to reduce the precautions needed for the operation and the time that the patient must be kept in bed. (2) Methods necessary for more advanced and complicated conditions.

(1) Under the first heading come the **percutaneous and injection** methods. Before the antiseptic period a pin was passed under the vein and a figure of eight ligature applied over the pin. Schede in 1877 used a silk ligature passed under the vein and tied over a roll of gauze. These were removed after 2 or 3 days like the pins, and the patient was supposed to be able to get up within a week. In 1915 Secher in Copenhagen, after marking out the veins with the patient standing up, administered a general anaesthetic and then passed a curved needle under the vein so deep as to take up a little of the deep fascia. The needle penetrated the skin, in and out, 4–5 mm. on each side of the vein, carrying a catgut ligature, which was then tied over the skin without interposing a roll of gauze. Much

pain was experienced for some days which was countered by morphia. The catgut sutures either fell off or were removed after a fortnight; the patient was kept in bed for two or three weeks.

From 1908 Kocher had used the following method. Under spinal anaesthesia a ligature was first applied to the internal saphena at its termination. Then a needle armed with fine silk which had been preserved in sublimate solution was passed through a fold of skin under the vein and tied without anything being interposed between the knot and the skin. Any number of these ligatures might be applied all over the leg. The patient was not kept in bed but walked about the same or the next day; the ligatures were removed after three days, two days proved too short a time, fourteen days too long. The patient could leave the hospital at the end of a week. There had been no contra-indications such as embolism; the essential thing was the disinfection of the skin. For this purpose he employed benzine and alcohol; iodine was found objectionable, as tending to set up erysipelas and eczema. Presumably the 10 per cent. solution of iodine was referred to, not the 2 per cent. solution used in this country. Subsequent dilatations can be similarly treated.

Amongst the various forms of injection that of Schiassi may be regarded as complicated and that of Zirn as simple. Schiassi of Bologna in 1913 said that with the patient under spinal anaesthesia, an incision was made just below the saphenous opening and the vein divided between a ligature on the proximal side and a clamp on the distal. A second incision was next made just below the knee and the internal saphena vein divided between two clamps. Then an aqueous solution of iodine was taken (iodine 1, iodide of potassium 10, water 100) a solution in water is essential. This solution is injected into the proximal divided end of the vein below the knee, the clamp having been removed, the injection is continued until the iodine solution begins to escape from the distal end of the divided vein in the incision just below the saphenous opening. After that both open ends of the vein are tied. A third incision is now made at the inner side of the ankle and the vein divided between a ligature on the distal end and a clamp on the proximal. Then, having removed the clamps, the iodine is injected into the proximal end of the divided vein beside the ankle until the solution flows from the distal end of the vein in the incision below the knee. After tying these two ends the skin margins are sutured, and the limb bandaged. The patient is able to get up after ten days, the iodine solution causes an obliterative inflammation, and by commencing with ligaturing the vein at the saphenous opening there is no danger of embolism.

Zirn claims simplicity for his method of intravenous injection of sublimate solution. The injection of a 1 per cent. solution of sublimate for syphilis had shown that it was very liable to set up a local thrombosis; hence arose the suggestion to use it during the war so as quickly to remove disability and to enable the man to return to duty. It was necessary as a preliminary to ensure that the patient was free from albuminuria, diabetes, arteriosclerosis and cirrhosis of the liver, also there should be no eczema or other disturbance of the skin of the leg. With the patient standing up a very fine hypodermic needle is entered through the skin above or below the varicosity to be injected. The needle is then pushed on for 1–2 cm. before entering the vein. The needle must be first proved to have entered the lumen of the varicosity by withdrawing a little blood, then 1–2 cm. of the 1 per cent. sublimate solution is injected and as the needle is withdrawn pressure is applied to prevent any escape of the solution into the subcutaneous tissue. The injected fluid should next be moved a little by massaging with the finger, and the thrombosis may then occur immediately or only after some hours. There was found to be no need for pressure on the vein above, for no signs of embolism arose. There is no pain beyond the puncture of the skin, so long as none of the solution leaks outside the vein. There follows a little induration and redness of the skin over the site of the injection for a few days. It is best to begin with thrombosing the internal saphena vein above the knee, whilst spots where the skin is thin over the varix should be avoided, and especially towards the ankle. After the injection the man can go back to his work and it is only exceptionally that he has to take to bed. Three-fourths of the cases became at once fit for active service. In some Landsturm men permanently unfit for active service, there had been no return of varicosity in the veins actually injected and which had become thrombosed and obliterated. If collateral branches become subsequently dilated they are injected later.

(2) Among the methods indicated for more complicated conditions is the modern adoption of the old method by which pockets of veins are plucked out through small incisions. Stadel followed Narath in recommending this procedure. The upper end of the saphena is first tied, then the short incisions are begun from above downwards; there is then no danger of embolism; no tourniquet is needed; blood escapes or can be squeezed out; thus subsequent thrombosis and haematomas are avoided. The incisions should be short and only enter the subcutaneous tissue; the scars will then be mobile after healing.

Since Mayo's recommendation in 1904 use has been made of his principle of enucleation of the internal saphena vein in the thigh by making two short incisions and passing over the vein his ring-ended enucleator. The vein so freed is torn out. Babcock in 1907, passed a knob-ended probe through the vein; some pass a probe carrying a strong silk ligature, one end of which is tied to the end of the vein. The vein is then dragged out without any preliminary separation. The procedure can be carried out on a straight dilated vein with an enlarged lumen. It cannot be easily practised if the change in the vein has been one of thickening of the wall tending to endophlebitis obliterans. Neither is it suited to the widely dilated vein tortuous at intervals. The objection to the method is the liability of the vein whilst being torn out to break off, and the tendency to the formation of haematomas which may be followed by persistent induration or even by suppuration.

Tamisiea gave an optimistic report of his experience with this method in France. Having applied a tourniquet, he made an incision an inch long below the saphenous opening and above the knee. A ligature was applied to the proximal end of the vein in the upper incision and to the distal end in the lower. Then he took a 40-inch length of stout pliable silver wire with a knob attached to one end, and passed it along the lumen of the vein between the two incisions. The leg being held straight, the segment of vein was torn out by drawing on the wire. There was little or no haemorrhage. Both incisions were sutured and covered with collodion dressing. The men were sent back to the front in 10–14 days free from the pain of which they had previously complained.

There is one condition in which a free incision extending the whole length of the thigh or leg is indicated because of the danger to life from rupture and haemorrhage. It is when the internal saphena vein has been allowed to become very dilated and tortuous, the walls of the varicosities having become exceedingly thin and adherent to the atrophied skin. Any attempt at enucleation necessarily results in tearing of the vein and haemorrhage. The skin of the thigh can be rendered aseptic and can be sutured; if this cannot be ensured in the case of skin of the leg, owing to eczema the wound should be left open, unsutured. The incision just through the skin should be made so as to expose and tie first the upper and lower ends. Then the skin over the intermediary portion is divided, the margins retracted and the tortuous dilated vein gradually separated, whilst collateral communications are clamped. A tourniquet should not be applied; it is not needed. The patient should be kept in bed until the wound is firmly healed.

Delbet's proposal, made in 1906, to insert the upper end of the saphena into the femoral vein is generally condemned as useless and liable to set up thrombosis.

Semicircular and circular incisions were first used for the relief of varicose ulcers. Gay in 1855 made lateral semilunar incisions 1½ inch from the margins of the ulcer down to the muscle. Nussbaum in 1873 made a circular incision around the ulcer 4–5 cm. from its margin.

Moreschi in 1894 adopted two incisions round the leg, one above the ulcer, and one below, just above the malleoli.

Rindfleisch in 1908 applied a spiral incision down to the deep fascia, as many as four turns of the spiral being made between the ankle and the knee. So close a spiral is a misapplication and tends to produce oedema of the foot, especially when the original procedure is followed, the wound being kept open by plugging with gauze and healing by second intention enforced. In women, especially, the leg and thigh, on one or both sides, may be found much enlarged by soft oedema, fat and minute venules with very thin walls scattered all over the limb, whilst forming in spots naevoid patches. For this condition the following modification of the Rindfleisch spiral should be carried out. The incision is begun over the saphenous opening where the upper end of the saphena is tied, then a spiral incision is made, turning over the front of the thigh so as to complete one turn of the spiral on reaching the popliteal space. The second turn of the spiral passes behind and below the internal condyle, across the upper third of the front of the leg, then turning round below the calf, it ends behind the internal malleolus. This double spiral avoids the condyles of the femur and the malleoli, also the prominence of the calf, spots where scars are subjected to irritation. The incision throughout its whole length should be carried down to the deep fascia, the margins retracted and the surface of the fascia scrubbed with dry gauze to ensure that transparent veins are divided. This done, there are very few veins to clamp and tie. The whole incision can be sutured and heals quite well. When the woman gets up a bandage should be worn for a time, until there is no further tendency to oedema.

In some cases of varicose ulcers Bircher scraped away the unhealthy granulations, then he cut the spiral so as to cross the ulcer. The incision was made down to the deep fascia and that part of the incision in the leg was made to heal by second intention so that the varicose veins were completely obliterated. As a result the ulcers became covered with vascular granulations which could then be brought to heal by epithelial grafting. On the other hand, this spiral incision proved useless when there were no varicose veins, the ulcers then showed no improvement from its performance.

Neglected cases become complicated by solid oedema passing on to elephantiasis, when disablement tends to become complete, so that no relief can be given except by amputation. Even this becomes impracticable when the elephantiasis reaches the upper part of the thigh.

Kondoléon of Athens began in 1912 to make longitudinal incisions through the thickened and oedematous skin down to the deep fascia, from which a strip was excised. The muscles then bulged forward and came into contact with the oedematous subcutanous tissue. In 1915 he reported the result in 10 cases of elephantiasis, the more successful ones being filarial in origin, 2 were cured; 3 importantly improved; 2 had healed but had not been heard of again: 1 recurred; 1, a case of enlarged arm following cancer of the breast, died of pulmonary embolism a week after the operation; 1 case, also of the arm consequent on mammary carcinoma was relieved so far as the oedema was concerned, but the pain in the arm was not improved.

Green and Sistrunk extended Kondoléon's method by including the skin in the incision, because after the subsidence of the oedema it was in excess.

Green gave reproductions of photographs to show the effect on a woman, both of whose legs were enlarged by elephantiasis up to the great trochanter. An accompanying diagram showed an incision commencing over the great trochanter; the incisions diverged from one another, so that at the middle of the outer part of the thigh they were 10 cm. apart; to the outer side of the external condyle the incisions approached to 6 cm. from one another; they diverged again at the middle of the outer side of the leg to be 10 cm. apart, and came together over the external malleolus. The intervening skin, thickened subcutaneous tissue, and deep fascia were excised together in one strip and the wound sutured. A second strip of a similar character was taken from the inner side extending from the lesser trochanter to the internal malleolus. Green's case was reported too soon for any conclusion to be formed. The leg was much reduced in size but there was a tendency to oedema on standing. Returning to the conditions of elephantiasis complicating varicose veins and varicose ulcers, it would seem that an application of Kondoléon's procedure may be a means of affording relief and of avoiding amputation.

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W. G. S.

CONTUSION AND TEMPORARY COMPRESSION SETTING UP ISCHAEMIC DEGENERATION OF MUSCLE

Accidents attended by extensive bruising and temporary compression of the limbs are followed by shock and end fatally. In the absence of more obvious injuries the death is commonly attributed to internal lesions. But without any such injury to the limbs as fracture, dislocation, or rupture of muscle, an acute degeneration of muscle may be set up, sufficient by itself to account for death. A local contusion of the external soft parts may be followed by spasm, extreme tenderness, and limitation of movement of the limb whilst there is an absence of signs of injury to bones, joints, or nerves. A partial degeneration of muscle explains the symptoms, which should be distinguished from the effect of a nerve or spinal cord injury.

Frankenthal described three cases with the object of directing attention to the importance of these injuries to muscle. In war they follow explosions, in civil life falls of earth and stones in mines and quarries. He noted that in Military Hospitals there were men suffering from contusions without obvious gross lesions such as fracture. The bruising had been followed by spasm, marked tenderness of muscle, and a persistence of impairment of movement.

Case I. A pioneer, aged 21, was crushed by the explosion of a mine; he was taken to a field hospital and at once injected against tetanus. The man was pale, his temperature 36·8° C., his pulse rate 120, he presented numerous abrasions and bruises; in the right temporal region there was a wound 3 cm. in length going down to the pericranium; examination of the chest and abdomen disclosed nothing abnormal, but the urine contained blood. The limbs showed no wounds but numerous red and blue patches with abrasions; there was no fracture, dislocation, or obvious rupture of muscle. All the limbs could be moved by the patient. The left lower extremity was markedly swollen, hard as a board, very tender to pressure; the femoral artery could be felt pulsating.

The right thigh was similarly swollen, mainly in the adductor region, also very hard and tender. There was an abrasion on the back of the left hand which was swollen, and the fingers could not be fully extended.

The patient had frequent vomiting, which lasted for 2 days, and so he was treated by continuous rectal infusion. The abnormal temperature and pulse-rate persisted. The only change was that the left limb became a little less hard. Then, on the 3rd day, collapse and death occurred. At the post-mortem examination the chief changes were a necrosis of the pancreas and an ischaemic necrosis of muscle together with small multiple haemorrhages in various places including the pituitary body. In the pancreas were several greyish yellow foci, varying in size from a linseed to a pea. One cavity in the tail of the pancreas, the size of a bean, contained greenish yellow fluid. The muscles of the thigh were partly unaltered—in some places there was extravasation of blood. But parts of the muscles were a greyish yellow in patches and strips, dry and friable, as compared with the unaltered dark-red tough muscle. The colour of the altered parts somewhat resembled salmon muscle. The blood-vessels were dissected out, but there had been no injury to them. There was no sign of fat embolism.

Case II. A private, as the result of a mine explosion, lay for a long while crushed by beams and masses of earth. There was a fracture of the lower end of the left radius, but none of the lower limbs. Both thighs showed bruises; the left thigh was swollen, tense, hard, and very tender; it could be moved to a limited extent. The colour of the man's face was blue, he appeared stunned and only answered slowly and with difficulty. The chest and abdomen were normal to examination and no other injury was discovered. The temperature was 36° C., the man failed to rally and he died about 12 hours after the injury. At the post-mortem examination no wound or injury to any large blood-vessel was discovered. The only definite internal lesion was a congestion of both bases of the lungs. The pectoral muscles exhibited the greyish yellow patches and streaks resembling salmon muscle; the same was found in the muscles of the left thigh. There were besides numerous scattered small haemorrhages.

Case III. There was no evidence as to how the man was injured. There was noted a laceration of the right ear, also numerous bluish patches over the body. The chest and abdomen were normal to examination, but the urine drawn off by a catheter contained blood. The pulse was small and thready, the face very pale, the temperature 37·5° C.; there was continuous vomiting, and he died about 9 hours after the injury.

There was found a partial rupture of the liver and spleen with infarcts from small injuries in the spleen, and in both kidneys, also fracture of the spine and ribs. The intercostal muscles exhibited a marked degeneration as above.

In a case observed by Pielsticker there was an absence of any lesion of the internal organs.

A woman, aged 42, fell in an epileptic fit with the right shoulder against a corner of a table. Five days later there was no sign of fracture or dislocation, but marked swelling of the right shoulder with intense tenderness. A recurrence of epileptic fits was followed by death ten days after the accident. At the post-mortem, there was found a fatty degeneration of the cardiac muscle. The blood was sterile. There was no other obvious cause of death except the condition of the right shoulder. The skin over the shoulder was tense, but not otherwise injured, there were several patches of bruising. The deltoid in particular, but also the pectoralis major, showed small extravasations of blood. Besides normal muscle and the above extravasations, there were spots and streaks of a dull greyish yellow colour, having an appearance of boiled muscle, also small wheat-like anaemic infarcts in a kidney. The degeneration gave a spotted and streaked appearance to the muscles.

In 1893, Rudolph Volkmann examined the condition of the muscles immediately above the line of demarcation of the dry gangrene which had followed frost-bite. As distinct from the normal dark-red muscle, he noted opaque yellowish and pale red patches and streaks which gave the muscle a peculiar marbled appearance. The colour was like that of salmon muscle. Muscle undergoing fatty degeneration has a brighter yellow look. On longitudinal section the degeneration was seen to form pale streaks in the course of the fibres ½ cm. or less in width. This change in the muscle was distinguished from that about the line of demarcation where the colour became a blackish-red with haemorrhages. Under the microscope the degeneration was seen to commence within the sarcolemma. One form resembled that occurring in typhoid fever, first a multiplication of the muscle nuclei, next a disappearance of the transverse striation, accompanied by an irregular fibrilation in the longitudinal direction, and then a separation of albuminoid and fatty particles which gave a granular appearance, together with vacuolation. Another form differed from the above by a relative absence of nuclear division and a retention of the transverse striation so that there was a tendency for the fibre to break up into Bowman's disks rather than into longitudinal fibrils.

This degeneration is distinguishable in its earliest stages from rupture of muscle fibres because the tube of sarcolemma is intact and the degeneration commences within. Another marked peculiarity is the early collection of irregular calcareous masses which take a deep stain such as were described by Schujenioff in 1897. The deposit depends on a local disturbance of the circulation among muscle fibres. He found similar deposits early around the sutures passing through muscle in wounds healing by first intention. Calcareous deposits appeared within 18 hours in wounds made experimentally on animals. The calcareous deposits tend to disappear in wounds healing by first intention, along with the disappearance by absorption of degenerated muscle fibres.

Ischaemic lesions may be produced by a temporary compression, (*a*) of the main artery of a limb or organ; this may include indirect compression by the forcible kinking of the main artery for a short while; (*b*) of the nerves, causing a spasm of the vasomotor apparatus. The result may be the production of multiple small haemorrhages which arrest the local blood supply. This explanation would account for the patches and streaks of ischaemic degeneration in muscle, also for those lesions of internal organs which cause infarcts, e.g. in the kidney, rather than actual ruptures. In cases, therefore, of severe contusions and temporary compressions degeneration of muscles of the limbs must be reckoned as an important factor in the causation of shock and death. In less severe cases, in which the lesion is local the degeneration of muscle accounts for extreme tenderness and impairment of movement. This will be followed by a regeneration of the striated muscle fibres commencing with a proliferation of the muscle nuclei as described by Volkmann. Recovery from tenderness and stiffness of muscle is dependent upon the progress of the regeneration.

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W. G. S.

APPARENTLY DEAD

'I must repeat,' said Marshall Hall, 'that hibernation is, in every respect, but the parallel of ordinary sleep, varying only in force and duration.' A London coroner recently blamed the bystanders for assuming that a man, just drawn out of the water, was already dead.

Rautenberg described a case which would have been buried alive, had it not chanced that the coffin was reopened for purposes of identification. The woman had been reduced to the state of a hibernating animal by an overdose of morphia and by cold. The doctor who examined her in the mortuary applied only one special test, that of dropping sealing-wax on the skin. He made no note of the state of the pupils, which were subsequently found contracted.

On October 27, 1919, a hospital nurse, aged 23, bought from an apothecary in Charlottenburg for 20 marks 50 c.cm. of a 3·5 per cent. solution of morphin, and 10 powders each containing 0·5 grms. of veronal. She then went into the Grünewald, and about 4 p.m. swallowed about 1·7 grms. of morphin and 5 grms. of veronal. She wandered about as in a dream until she lost consciousness. The weather was cold, the temperature during the night being 1–3° C., and wet.

When she was found the next day, she was assumed to be dead and was taken to a mortuary, where the Medical Officer of the District examined her. The body had a deathly pallor; there was an absence of pulse, of respiratory movement, of the heart sounds, and of all reflexes. There was partial stiffness of the trunk and limbs, and it was assumed that rigor mortis was as yet incomplete. There was no reaction to sealing-wax dropped on the skin. There is no mention of the state of the pupils. After the examination, the body was put in a coffin, still in the wet clothes. 14 hours later, on October 29, the coffin was reopened in order that a lawyer might identify the body. The undertaker's men then noted that the cheeks were coloured blue and that there was a slight movement of the head. The same medical officer was again called and now heard faint heart sounds, but there was still an absence of a pulse and of respiratory movement. The patient was then moved to a hospital, when at 10 a.m. on the 29th, i.e. 42 hours after the poison had been swallowed, it was found that the trunk and limbs were partially stiff, that she was unconscious and that there was no reaction to stimuli. The double heart sound could be heard over the sternum, the heart beating 30–40 a minute; signs of breathing, and of a pulse were absent. Both pupils were markedly contracted. The skin and lips were deadly pale, but the cheeks were bluish (*leicht cyanotisch*). The stomach wash contained morphin; the urine drawn off from the bladder, besides albumin and casts, also contained a small quantity of morphin. Under active treatment for morphin poisoning, the stiffness of the limbs began to pass off in 2 hours; consciousness began to be regained on the 30th. On November 3, the patient was convalescent and the urine free from albumin. No pneumonia or other complication supervened.

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W. G. S.

ELECTRIC INJURIES

Those who escape death from lightning or electric stroke present, as distinguished from burns, peculiar injuries, one a slow dry gangrene of the skin, and another a spreading, also dry, gangrene of the limb. In the case described in 1905 by Lucas, severe burns and arrest of the circulation in all four limbs was produced, so that moist gangrene followed. Jellinek, in Vienna, has continued to give attention to this form of injury, and the two cases he has recently described may be distinguished from burns; also the main circulation in the affected limb was not at first disturbed. He cites the two cases as illustrating the advantage of conservative over operative treatment. The course taken by these electric injuries is very similar to that following frost-bite.

Case I. A man, aged 35, engaged in an electric power house, on June 23, 1917, approached with his right forehead too near a current of 35,000 volt tension and 48 per sec. frequency, whilst his right elbow was in contact with the ground. There was no witness of the accident, and he himself was not conscious of it until he had descended from the third to the first floor. There his fellow workman noted blood-stains on his right forehead and left ear. He thereupon went up alone to the third story and wiped up from the floor some blood. All that he could remember was that, shortly before the accident, a comrade had gone to fetch his dinner, and that he had been called to the telephone and told that his dinner had been brought. The man was taken to Jellinek 1¾ hours after the injury. He then presented no general signs, and readily accepted, with an appetite, an invitation to a meal. His injuries were photographed and a water-colour sketch made, but the appearance of his forehead and his right elbow were the only evidences of his accident. The forehead had the general appearance of abrasion and suffusion. Over the right frontal eminence, within the hairy margin, there was a bare, greyish-white, circular patch, the size of a crown piece, level with the normal scalp. This was surrounded by a ring of suffusion, from which the epidermis had been detached, and the corium exposed. Around the bald patch the hair had been singed; in the middle of the greyish-white area were several depressions running into one another, some 2 mm. in depth, dry, and dusky brown in colour.

On the extensor aspect of the right elbow-joint were irregular streaks, greyish-yellow or brown in colour, from which the epidermis had been for the most part detached. Around were stellate areas injected red. On the back of the right hand there were abrasions and suffusion. The pulp of the right index finger exhibited a circular greyish-white hard elevation of the epidermis, larger than a hazel nut, insensitive and without redness around.

The next day the area on the forehead, the size of a crown piece, was dry and unaltered, the surrounding ring was markedly red. The exposed corium over the elbow was discharging freely. The finger was unaltered. There was no general disturbance or pain.

The patch on the forehead increased somewhat in area, and underwent dry gangrene; on July 12, the 19th–20th day from the accident, the slough was cut through in order that pus underneath might escape. On July 23, the slough of the scalp and pericranium separated, exposing bone the size of a farthing. The bone was dry; there was no pain, or tenderness on tapping the skull. Granulations and a thin layer of epidermis made attempts at covering over the bare skull, but there were several relapses, and it was not until January 1918, six months after the accident, that the area was covered by a firm painless scar, level with the rest of the scalp and without sign of contracture. There had been no exfoliation of the outer table of the skull. The injury at the elbow extended by sloughing at its margin, but the corium was not penetrated; it became covered with granulations, and then by epidermis in about six weeks from the accident. A central slough formed in the pulp of the finger, which was detached, and healing followed without exposing the phalanx.

. *Case II.* A boy aged 17, barefoot, climbed the iron mast supporting the cable of an electric railway, and seized with his bare left hand the cable carrying a current of 16,000 volt tension and 48 per sec. frequency. At that moment he was holding himself to the mast by his right arm and the insteps of his bare feet. He felt no pain, only that he could not release himself; then he became unconscious. He was taken to hospital unconscious, groaning continuously, crying out from time to time, restless; he had passed both urine and faeces. Two hours later he was so restless that it took four nurses to hold him in bed until he was quieted by morphin injection. On the third day he was partly conscious and told a story of the horses of a wagon in which he was sitting having run away, when he had grasped the electric cable with his hand. But later on the same day he gave the correct account, saying that he could remember up to the moment of seizing the cable. He had then no pain, was hungry, and wanted to smoke. His left hand and arm appeared severely injured, the hand swollen, yellowish black and brown; there was an extensive destruction of the palm, the metacarpo-phalangeal joints of the 4th and 5th fingers were laid open, the fingers hanging by brownish strips. The forearm and arm were diffusely swollen, the skin brownish with numerous, mostly streak-like depressions with reddened surroundings, but all painless. He could move his wrist, elbow, and shoulder; in particular there was some flexion and extension at the wrist. The radial pulse was plainly felt. The right hand had not been obviously injured, but, owing to some median and ulnar paresis, the fingers could not be fully flexed to make a fist, nor could they be readily abducted and adducted. There was no loss of sensation. Around the middle of this arm was a ring 5 mm. in breadth, with several depressions from which the epidermis had been detached in a stellate manner, yellowish-red and brown in colour, dry, painless, insensitive to touch and pin-pricks. The surrounding skin was a little reddened; the rest of the forearm and arm retained normal sensibility.

The right great toe had on the inner side of its nail a dry brown patch the size of a pea, painless, and without redness around. In it was a central depression 1 mm. deep, of a brownish colour and dry. Over the right internal malleolus, there were superficial injuries, partly true electric injuries, partly burns. Within the area of true electric injury the fine hairs of the skin were unaltered and these areas were painless. There were similar injuries over the left instep; only the burns were painful.

On the fourth day from the accident the patient presented little evidence of general disturbance; he held up his badly injured left arm and hand in the position required by the photographer without pain, and the radial pulse could be felt. But on the fifth day from the accident the radial pulse began to disappear and a slow process of dry gangrene and mummification set in, with the formation of a line of demarkation about the level of the insertion of the deltoid muscle. This slowly deepened down to the bone, along with retraction of the soft parts above. In the fifth week the X-rays showed a commencing line of demarkation in the humerus; a fracture occurred during the sixth week and the gangrenous arm separated spontaneously. Four months later the projecting bone was shortened.

The great toe healed after the separation of a central slough. The right arm developed more complete paralysis of the median and ulnar nerves, with loss of faradic reaction, but after four weeks gradual recovery set in. The superficial ring round the middle of the right arm slowly sloughed down to the deep fascia, then granulated and healed spontaneously in a month, the scar not adhering to the muscles, or showing any tendency to contract.

Jellinek added an instance of an injury to a horse. The left forefoot of a horse came into contact with the loose end of a 1·5 mm. telephone wire which had become broken and was hanging down over the bare cable of an electric tramway. The horse was rendered deeply unconscious, with a subnormal temperature, but without sign of any particular injury. The next morning the animal was trying to get up; it was then raised by slings, when it was noted that it did not bear weight on the left forefoot. The fetlock was found somewhat indurated; it was cold, not painful or oedematous. The hair, which was not singed, was shaved off, but no change in the skin noted. It was not until after four days from the accident that a discharge occurred from the back of the limb, on which the horse was then apparently bearing weight. There followed a sloughing which exposed the flexor tendon, the ligaments and the branches of the radial and ulnar arteries, and there commenced a separation of the hoof. The horse was again slung up, and during the seventh night there was such severe haemorrhage that the animal was rendered weak, and this, with the separation of the hoof, led to its being slaughtered.

According to Jellinek, the specifically electric changes in the skin are detachments of the epidermis in patches, strips, or points, producing a surface which is pale white or greyish in appearance, and this change may extend more or less deeply through the cutis. If the epidermis is simply raised from the cutis, there appear also depressions greyish black or bluish. There is around a fine whitish zone, but an absence at first of red reaction. When the epidermis is not detached, the surface is dry and there is little sign of any recent injury. A linear streak may have the appearance of an incised wound healing by first intention. The marked peculiarity of these electric injuries proper is the absence of pain; the area is insensitive both to touch and pin-pricks. The subsequent process is that of dry gangrene without suppuration and without general signs of septic absorption.

During the process of healing there is a varying extension of the area injured over that apparent at the first. There is desquamation of the epidermis or sloughing of the skin around, which at first seemed to have escaped injury. This is followed by rapid formation of granulations, and the area soon becomes covered with a new skin which is well supplied with blood, is soft, and mobile upon the deep structures. It does not undergo contracture later. The destruction may be so superficial as not to destroy the hair follicles, e.g. of the scalp.

The difference between a specifically electric injury and a burn is explained by human skin presenting a special resistance to the passage of the electric current, whilst the tissues of the body generally underneath the skin have merely a minimal resistance. In its passage through the skin, the electric current develops heat but merely at the surface of entry and of exit. If the current is sufficient, the heat destroys the skin, but as hair is a non-conductor it may be insufficient to destroy the hair follicles. On the other hand the heat developed may be intense enough to destroy by spreading to the tissue around the points of entry and exit of the current. The damage done can only be recognized when the case survives for several days. It is impossible to recognize the full extent of the injury on a dead person; the injury is obscured by changes in the tenseness of the skin and by the onset of putrefaction. The examination of the clothing and of the shoes, for most accidents happen whilst there is contact with the earth, also close inspection of the part of the body which has been in touch with the electric current, aided by a magnifying lens, are of importance. The true electric injury is independent of the character of the current, continuous or alternating, and there is no difference between the point of entry and that of exit. If it happens, whether at the making or breaking of the current, that a spark is formed, a burn is caused and then the injury has a mixed character, a burn is superimposed upon the electric injury proper. There may also be changes dependent on electrolysis: thus contact with a copper wire may result in a bluish-green staining of the skin, due to a combination between copper and a fatty acid. An electrolytic process under the skin affects the blood-vessels, causing spasm and then paralysis of the vasomotor apparatus which is followed by progressive thrombosis. This change in the arteries contra-indicates early amputation, for recurrent uncontrollable haemorrhage from the stump has followed and ended fatally. Indeed the thrombosis may be followed by embolism; a case in which the axillary artery became thrombosed after an electric injury was complicated two months later by cerebral embolism causing hemiplegia. The thrombosis renders the administration of a general anaesthetic a danger, and the reason against early surgical interference is the difficulty of then estimating the damage done. Parts may recover which at first appear to be going gangrenous. On the other hand, the impairment of the wall of small blood-vessels favours sloughing of the margins of an operation wound including the flaps of a stump.

Among more than 100 cases, the rigid adherence to a conservative line of treatment has been attended with success. Among the cases which had survived the first effect of the injury, only one died from numerous burns received in addition to the true electric injuries.

Lucas, R. C. A case of accidental electrocution causing extensive gangrene of all the extremities and death on the ninth day. *Tr. Clin. Soc. Lond.*, 1905, **38**, 86.

Jellinek, S. Die Eigenart der electrischen Verletzung und ihre ärztliche Wertung. *Wien. klin. Wchnschr.*, 1918, **31**, 1173, 1207.

W. G. S.

ABSTRACTS

NEUROLOGY

FOERSTER, O. Die operative Behandlung der spastischen Lähmungen (Hemiplegie, Monoplegie, Paraplegie) bei Kopf- und Rückenmarkschüssen. [**The operative treatment of spastic paralysis (hemiplegia, monoplegia, paraplegia) resulting from gun-shot wounds of head and spine.**] *Deutsche Ztschr. f. Nervenh.*, 1918, **58**, 151.

The operative treatment of spastic paralysis is a problem which was occupying considerable attention in the days before the war. At the present time the question has become one of considerable moment owing to the many severe and lasting spastic paralyses which have resulted from wounds of the brain and spinal cord. Foerster, of Breslau, in a comprehensive paper, describes the common forms of these paralyses, with special reference to the exact types of spastic disabilities, the power of movement in different muscle groups, synergic movements, and the various operations applicable in the different cases. He begins his account with a detailed description of four patients upon whom he performed (no surgeon is named) *his central operation, section of the posterior nerve roots.* He believes that this severe manœuvre is called for only in those cases where no success is to be expected from other less energetic measures. It is not the method of choice in partial paralysis, in hemi-sections of the cord, where one leg has more or less escaped, but is indicated in severe bilateral spastic paraplegia with more or less total abolition of voluntary movement.

In his earlier cases Foerster used to remove the laminae of all five lumbar vertebrae and one-third of the hinder wall of the sacral canal. He has now adopted the modifications suggested by Wilms, Codivilla, van Gehuchten and others, and finds that it suffices to perform a laminectomy on the eleventh and twelfth thoracic and first and second lumbar vertebrae. This gives good exposure of the lumbo-sacral enlargement and of all the roots springing from it. The disadvantage of the restricted bone removal is that one does not know exactly which roots one is dividing. He finds, however, that it is quite satisfactory to resect from one-half to two-thirds of all the roots seen, cutting one or two, leaving one intact, cutting the next, and so on. If necessary the operation may be done in two sittings, the dura being exposed first, and opened at the second sèance a week or ten days later. Foerster is delighted with the results; not only is all spasm completely and permanently removed, but voluntary power returns within wide limits. The first case, as it illustrates well the type of paralysis suitable for posterior root resection, will be transcribed at some length.

Rifle-bullet entered three finger-breadths below the angle of the left scapula, exit two finger-breadths distant from the spine of the first thoracic vertebra. Immediate complete paralysis of both legs and the bladder. Loss of sensation up to the nipple level. When examined ten months after the receipt of the wound the patient lay in bed with the thighs tightly pressed against one another in slight flexion and internal rotation, the knees strongly extended, the feet in extreme equino-varus, and all toes, especially the great toes, strongly dorsi-flexed. Invincible spasm of the calf-muscles, extension of knee, adductors, extensors, and rotators of the hips was present. Patella and ankle-clonus + +. Babinski +. Deep stroking of sole of the foot caused a quick defence movement, a flexion of the legs which sometimes lasted an hour and could only be relieved by patient massage of the muscles of the thigh. Tendon reflexes + +. Sometimes the patient could bend the right leg at the hip and knee. This he did by rubbing the right thigh slightly against the left (the two being already tightly pressed together), or by pressing the two thighs still harder together. This was sometimes followed by a rapid involuntary defence movement of the right thigh. Complete anaesthesia and analgesia to the level of the nipples. Patient can stand only if he is powerfully supported on either side.

Operation: dura exposed from eleventh thoracic to second lumbar vertebra; two-thirds of the posterior roots of both sides of the lumbo-sacral enlargement divided. Immediately after the operation all spasm disappeared, and in fourteen days active movement, in the sense of extension and flexion, was present though ataxic. One month afterwards the condition was as follows: legs in good position at rest, feet in mid-position between flexion and extension, no supination. Knee in extension, no adductor spasm. Passive movements possible in full range without a trace of spasticity. Tendon-jerks absent. Bakinski +. Defence movement as before but without tonic continuation. Voluntary movements good: voluntary dorsal and plantar flexion of the feet in full range, powerful, without synergy at knee and hip. Flexion and extension of the thighs good, ataxic, powerful. In the sitting posture strong extension of the knees possible in full range. Raising of the extended legs from the bed possible to a slight degree. Adduction and flexion at the hips very strong, voluntary abduction and rotation only slight. A little incontinence of bladder and rectum. Skin anaesthesia as before. The patient can walk by himself with two sticks for several hundred metres.

One other such case of spinal injury is described, and then two very similar ones following bilateral injuries to the motor area, the clinical picture being that of Little's disease. Foerster wishes to call special attention to those cases where an interference with bladder control has followed an injury to the upper end of the pre-central area. At first catheterization is necessary and later on detrusor weakness persists. These cases, in his opinion, point to the existence of a cortical bladder centre (vide *Medical Science*, 1920, **1**, 506). The spastic paraplegia in Case 3, resulting from a bullet wound of the vertex, was greatly improved by root division as far as spasm was concerned, but voluntary power was not good owing to the destruction of motor cortex. However, after the operation, he was able to sit by himself and walk if supported, whilst before he had been helpless with iron-like muscle rigidity.

Foerster passes on to consider the *peripheral operations* which are applicable to single spastic limbs. In the first line comes tendon-lengthening. He condemns tenotomy unreservedly, believing a careful plastic lengthening, on the lines of Biesalski's work, to be greatly superior. This is particularly the case with the tendo achillis; he recommends a very oblique antero-posterior cut in place of the more usual method. He points out that tendon-lengthening can be equally well applied to the hand, especially to flexor carpi radialis, flexor carpi ulnaris, and palmaris longus.

An alternative method is Stoffel's procedure, the partial resection of motor nerves. Lorenz had already applied this to the obturator for adductor spasm, and Spitze injured the median for spastic paralysis of the hand and fingers, but Stoffel has worked out the technique in great detail. This is an operation which must be used with great caution. Unless considerable injury is inflicted on the nerve no amelioriation will accrue. and if a number of nerve-bundles are divided the already palsied hand is left worse off than it was before. Nevertheless the operation has its place, its special field of application being those muscles which are deficient in tendons, such as the adductors of the thighs, coraco-brachialis, pronators, brachialis anticus, and biceps in the arm. Lastly, tendon transplantation has to be considered. Foerster is not impressed with the results of transplanting the tendo achillis to the dorsum of the foot and thinks tendon-lengthening here is better. He has had very good results with the quadriceps femoris and tibialis anticus.

Considerable space is devoted to a discussion of the most suitable method of treating the severe equinus and supination of the foot which these spastic cases so frequently present. For this deformity he resects the motor branch to the tibialis posticus in the popliteal space, leaving only a quarter of the thickness of the nerve, and transplants half the tibialis anticus to the outer border of the foot.

For claw toes he resects the branch of N. tibialis to the flexor longus digitorum and sometimes tenotomizes the tendons as well. He has had excellent results by resecting the branches of the anterior crural nerve to the quadriceps, when the spasm of this muscle prevents flexion of the knee. A typical operation on a spastic monoplegia of the leg would consist of plastic lengthening of the tendo achillis, resection of the nerve-bundles to the tibialis posticus and flexor longus digitorum, stretching of the tendon of the tibialis anticus, and transplantation of half, partial resection of the nerve to the quadriceps extensor cruris.

The monoplegic arm, usually presenting contracture of the long flexors and adductors, with corresponding limitation of extension and abduction, presents peculiar difficulties. Any interference with the main nerve-trunks is not to be thought of, lest the last state be worse than the first. The finger flexion is best dealt with by partial resection of the branches of the median and ulna nerves to the flexores sublimis and profundus digitorum. Care must be taken not to divide too much, one-third is quite sufficient. It is advisable to tease out the nerve-bundles first, and then select a few fibres for division, otherwise it is quite possible to paralyse one finger completely and leave the others as spastic as before. The thumb contraction is dealt with in the same manner, with the addition of tenotomy of the adductors from the inner sesamoid bone. Transplantation of the flexor carpi radialis into the tendon of the extensor brevis pollicis gives as good results in hemiplegic cases as in peripheral nerve injuries. Plastic lengthening of the flexors carpi radialis and ulnaris with the palmaris longus overcomes the flexion of the wrists. For spastic contracture of the pronator radii teres Foerster recommends resection of its motor branch from the median, and for spasm of the flexor group of the upper arm section of one-third of the musculo-cutaneous nerve. Contracture of the latissimus dorsi and pectoralis major is best dealt with by division of the motor branches to these muscles, the brachial plexus being exposed above the clavicle. This has proved more satisfactory than operations upon the tendons of the muscles. The internal rotation caused by the subscapularis was first attacked by freeing of the tendon from the lesser tuberosity of the humerus, but experience has shown that resection of the greater part of the subscapular nerve is the better treatment.

The results of these operations are considered in detail; 12 further cases are described in detail illustrating the application of the methods in arm and leg, with 26 photographs illustrating various palsies.

It is noteworthy that Foerster lays little stress on muscle re-education and training, methods which are meeting with considerable success in this country for some of the cases on which he advises operation.

G. J.

Hall, G. W., Russell, J. C., and Holmblad, E. C. Further observations on the presence of arsenic in the spinal fluid. *Arch. Neurol. & Psychiat.*, 1920, **3**, 631.

In previous observations Hall, Schlegel, and McNally found that the cerebrospinal fluid withdrawn twelve hours after an intravenous injection of a salvarsan preparation contained arsenic, but that after twenty-four hours none could be detected.

In the present paper a new technique is described designed to facilitate the passage of arsenic into the cerebrospinal fluid after intravenous injection. The essential feature of this appears to be a preliminary intrathecal injection of from 10 to 15 c.c. of the patient's own serum, followed several hours later by an intravenous salvarsan injection. They found that 0·6 gr. injections in these circumstances were followed in from 25 per cent. to 35 per cent. of cases by the presence of appreciable amounts of arsenic in the cerebrospinal fluid. The preliminary intrathecal serum injection was therefore without effect, since in their earlier series the percentage was the same.

F. M. R. W.

Cobb, S. and Scarlett, H. A report of eleven cases of cervical sympathetic nerve injury, causing the oculopupillary syndrome. *Arch. Neurol. & Psychiat.*, 1920, **3**, 636.

The paper contains a short historical review of cervical sympathetic injuries, an anatomical and physiological introduction and case reports. Of the 11 cases described, 2 were lesions of the lower cervical roots, 4 involved the cervical sympathetic trunk, 4 were contusions of the cord in the region of the eighth cervical and first dorsal segments. In the last case the site of the lesion was not certain.

Reviewing their results, they find that (1) Enophthalmos was the most constant symptom and was most pronounced in the cases of root lesion. (2) Myosis and some ptosis were present in all but 2 cases. (3) Unilateral anhidrosis was present in 6, and vasomotor disturbances in 2 only.

On the whole, lesions of the seventh and eighth cervical and first dorsal roots produced the most severe symptoms, and in these the pupils did not dilate with cocaine.

F. M. R. W.

Hassin, G. B. Histopathology of brain abscess with remarks on intra spinal therapy. *Arch. Neurol. & Psychiat.*, 1920, **3**, 616.

From his observations on the morbid histology of cerebral abscess Hassin draws some significant conclusions as to the physiological foundations of intraspinal therapy in affections of the brain and meninges.

The capsule of long-standing abscesses may be extremely thick and three layers can be distinguished; an inner composed almost exclusively of collagen fibres which is poor in blood-vessels and cellular elements, a middle layer largely cellular in structure and consisting of masses of plasma and gitter cells, fibroblasts, and masses of fat granules. The outer layer contains both collagen fibres and the cells found in the middle layer. It appears that this capsule acts as an excellent protection for the surrounding brain tissue, which shows changes in its vessel walls but none of the nervous elements. There is marked proliferation of the adventitia, but the lumen, intima, and media of the vessels are normal. In the perivascular space of Virchow-Robin, in the vessels round the abscess, there are numerous plasma cells and cells containing fat granules. This adventitial cuff surrounding the vessels represents an extinct inflammatory process.

The pia-arachnoid is normal and not infiltrated with cells, but the subarachnoid space contains numerous macrophages, plasma cells, gitter cells, and more or less altered lymphocytes and fat granules.

Hassin concludes that normally the contents of the perivascular spaces flow from the brain into the subarachnoid space and that there is no flow in the contrary direction—that is, from subarachnoid space into brain tissue. The experiments of Weed, Spina, and E. Foerster also point to this conclusion. It is at least doubtful, therefore, whether the brain ever takes up substances, either formed elements or substances in solution, from the subarachnoid space, and if this be so there can be no sound foundation for intraspinal (intrathecal) injections in parenchymatous syphilis of the brain, though it may be rational to treat meningitis in this way. Such good results as some observers have reported from the Swift-Ellis treatment may depend upon the preliminary intravenous injection which would reach the meninges just as readily as an intrathecal injection. F. M. R. W.

Ehrenberg, L. Om lumbalpunktionsfyndet i åtta fal av opererad, primär ryggmärgstumör, med särskild hänsyn till lymfocyttalet og liquortrycket. [**Lumbar puncture findings, with special reference to lymphocytes and pressure, in eight cases operated on for primary tumours of the cord.**] *Hygieia*, 1919, **81**, 970–81.

Ehrenberg's paper is an attempt to establish a relation between certain lumbar puncture findings and tumours of the cord with signs of compression. To what extent, he asks, is Nonne's compression syndrome (increase of the albumin content of the cerebrospinal fluid, xanthochromia, no increase in the number of lymphocytes) a reliable sign in the differential diagnosis of various diseases of the cord? In 8 cases he performed lumbar puncture in the recumbent position before operation. In 5 the first dorsal segments were involved, in 3 the cauda equina. In all the 5 dorsal cases there were signs of compression. Only when these were comparatively slight was Nonne's syndrome unequivocally demonstrable. Lymphocytosis and xanthochromia occurred only in those cases in which the tumour of the cord proved to be exceptionally large. This would suggest that both these conditions depend on the degree of intraspinal occlusion. The degree of the globulin reaction also seemed to coincide with the extent of the intraspinal occlusion.

With regard to the pressure of the cerebrospinal fluid, when the tumour was higher than the site of puncture, the pressure was normal in 2 cases and below normal in 4. In the case of a much debilitated woman of 75, the globulin reaction was negative, and the pressure was so slight that the fluid only just oozed out. In 2 cases in which the pressure was below normal to begin with, the withdrawal of only a small quantity reduced the pressure to a marked degree. Ehrenberg regards this sudden fall of an already low pressure, after only a small quantity of fluid has been withdrawn, as a valuable sign of compression. He is reserved in construing general rules on the basis of his 8 cases, but he suggests that in uncomplicated cases of compression of the cord by tumour, Nonne's syndrome should include a moderate degree of lymphocytosis. He sees in this lymphocytosis a sign that promises to be of importance in the differential diagnosis of tumour-compression and other morbid changes in the cord. C. L.

Zethelius, M. Lumbalpunktion såsom behandlingsmetod för synnedsätning, framkallad genom akut metylalkoholförgiftning. [**Lumbar puncture in the treatment of methyl alcohol amblyopia.**] *Hygieia*, 1920, **82**, 45–52.

Zethelius publishes 3 cases of ocular disturbances provoked by methyl alcohol poisoning, in which he achieved a striking improvement in 1 case, considerable improvement in another, and some improvement in the third by repeated lumbar puncture. He is the more impressed by the value of this treatment as the conventional treatment with potassium iodide and diaphoretics is unsatisfactory. He suggests that the action of lumbar puncture in these cases may be twofold. Methyl alcohol having been found in the cerebrospinal fluid of persons dying from its effects, it is probable that lumbar puncture withdraws methyl alcohol and its decomposition products from dangerously close contact with the central nervous system. Secondly, a reduction of the intracranial pressure may limit the absorption, by the central nervous system, of poisons in the cerebrospinal fluid; this hypothesis is the more plausible as in the first case recorded by Zethelius the pressure of the cerebrospinal fluid was abnormally high. C. L.

Saelhof, C. Multiple brain abscesses secondary to bronchiectasis and kyphoscoliosis. *J. Nerv. & Ment. Dis.*, 1920, **51**, 330.

A case of multiple bilateral cerebral abscesses secondary to a bronchiectasis of the right lung, said to be due to the compression of this by a kyphoscoliosis. The *B. fusiformis* was isolated from lung and abscesses and the latter were probably haematogenous. F. M. R. W.

Macklin, C. C. and **Macklin, M. T. A study of brain repair in the rat by the use of trypan-blue.** *Arch. Neurol. & Psychiat.*, 1920, **3**, 353.

The basis of the method employed is the use of 'vital staining'. An aseptic lesion of the brain is produced by plunging a fine red-hot needle into the brain substance and withdrawing it instantaneously. The rat is then kept alive for varying periods so that the different stages in the reaction may be studied, and 48 hours before it is killed by bleeding, 4 or 5 c.c. of a 1 per cent. solution of trypan-blue are injected intraperitoneally.

The brain is a particularly favourable organ for the use of this method, since the tissue is white and contrasts well with the dye, and since it contains no cells which under normal conditions take this up. Thus any dye taken up in the inflammatory area round the lesion is very conspicuous. The vital dye is taken up readily by the mononuclear lymphocytes which throng the inflamed tissues and is seen as fine droplets or granules, and it is the affinity of these cells for finely particulate matter which has gained for them the name of ‘ macrophages ’.

The effect of the heating is to sear a cone of tissue immediately around the needle. This cone or coagulum pulls away from the surrounding tissue into which steam is forced. Thus an intermediate zone is formed into which blood and exudate penetrate. Around this zone is a necrotic wall of brain tissue in which the vessels are thrombosed. The inner and outer zones stain deeply, the intermediate zone a paler blue. The staining reaches its maximum by the sixth hour and retains its intensity for three days, after which it fades progressively. The tissue in the region of the lesion also shows some staining, and this the authors think may correspond with the area of oedema, for the dye is intercellular and not within the cells in this peripheral zone.

Microscopically, all cells in and within the necrotic wall of the lesion are destroyed and are found in various stages of dissolution as we pass out from the centre of the lesion. In the zone peripheral to the wall it is found that nerve cells are more severely and extensively injured than the cells of the supporting tissues.

Repair : The injured area is rapidly invaded by a form of granulation tissue arising in the vessels and in the pia. Fibroblasts, macrophages, and vascular sprouts take possession of the entire area. The destroyed matter within the necrotic wall is rapidly absorbed, and soon a sheath of cells forms between the necrotic material and the tissue that is going to recover. Fibroblasts and macrophages constitute this at first, and it rapidly becomes a definite membrane which is well marked by the fifteenth day. Within this isolating membrane a fibrous scar forms.

Fully developed macrophages were present in the lesion from the second day onwards. They were most active during the first week after injury and they varied in diameter from 7 to 42 μ. They contained much lipoid material and some blood pigment. When compared with the macrophages occurring in other tissues than the brain, those seen were remarkable for the small amount of dye they took up, and the short period over which they took it up. In the brain they seem more actively phagocytic for fat and blood pigment than elsewhere. No forms transitional between fully formed mononuclear cells and lymphocytes were found, and there was evidence of mitotic division at the site of the lesion. They were apparently developed in part, at least, from neuroglial elements and in part from vascular endothelium. Their function is apparently to ingest the products of tissue destruction, which they subject to a form of digestion. Some of them were incorporated in the scar tissue.

The paper contains a wealth of detailed information, but owing to defective arrangement it is difficult to form a very lucid conception of the various degrees and stages of the process described. F. M. R. W.

PATHOLOGY AND BACTERIOLOGY

NICOLLE, CH., GUENOT, A., et BLANC, G. Reproduction expérimentale du trachoma. [**Experimental reproduction of trachoma.**] *Compt. rend. Acad. d. sc., Par.*, 1920, **170**, 642.

The trachoma virus is brought directly from patient to scarified conjunctiva of rabbits. Lesions are produced which, though not pronounced, are such as to be easily recognizable and comparable with those of trachoma. The incubation period is from 11–13 days, the eruption granular and generalized, very often in placques. The granulations persist at least 60 days, after which time they undergo spontaneous cure. Curetting does not hasten the cure. The rabbit virus has been inoculated with positive results on *Macacus cinicus*, which animal is known to be receptive for such a virus. A. D.

HAMBURGER, FRANZ. Zur Pharmakologie des Tuberkulins. [**On the pharmacology of tuberculin.**] *München. med. Wchnschr.*, 1920, **67**, 480.

The author, well known for his researches on tuberculosis in children, laments the fact that during and since the war a number of publications on tuberculin evince a lack of knowledge of results which he contends are well established. He sums up the actions of tuberculin under six heads:

(1) Tuberculin is non-toxic in tubercle-free persons, and a sensitization of such persons by tuberculin does not occur.

(2) Tuberculous individuals are always sensitive to tuberculin in some degree or other.

(3) In spite of the 'cure' of tuberculosis, tuberculin susceptibility persists throughout life.

(4) The febrile tuberculin reaction often induces an immediate loss of tuberculin susceptibility which may endure for 3 to 4 days (negative phase).

(5) On the other hand, the application of tuberculin usually causes an increase in sensitivity lasting 4 to 7 days (positive phase).

(6) Tuberculin susceptibility varies not only in different persons but in one and the same individual at different times. W. B.

HASLAM, T. P. and FRANKLIN, O. M. Experiments on immunization with pseudo-blackleg pellets. *J. Infect. Dis.*, 1920, **26**, 424.

The authors have investigated the strength and composition of various vaccines employed in the prevention of symptomatic anthrax ('blackleg'). In a previous paper (*J. Infect. Dis.*, 1916, **19**, 408) they showed that a certain commercial brand of blackleg vaccine supplied in pellets contained not the *Bacillus chauvoei* as it ought to have done, but another anaerobe which they designated as the pseudo-blackleg bacillus. The latter differed from *B. chauvoei* in being pathogenic for rabbits, in the formation of a putrid odour, in its gas formula, the appearance of the colonies, the blackening of ferrous-sulphate agar, and in the fact that guinea-pigs protected by true black-quarter vaccine succumbed to a subsequent inoculation of the pseudo-blackleg cultures. Injections of blackleg immune serum also failed to protect guinea-pigs against pseudo-blackleg cultures. In the present paper the authors have extended their experiments to calves and have found that although inoculated with pseudo-blackleg pellets these animals were not immune to true blackleg virus. All calves treated with true blackleg virus were found to be immune when subsequently tested with the same virus in a dose which killed control animals. The confusion in regard to the bacteria of symptomatic anthrax has already been emphasized by the Anaerobic Committee of the Medical Research Council in their report (*Special Rep. Ser.* No. 39, p. 23). W. B.

Levaditi, C. et **Harvier, P.** Recherches expérimentales sur l'encéphalite léthargique. [**Experimental researches on lethargic encephalitis.**] *Compt. rend. Soc. de biol.*, 1920, **83**, 674.

In a preceding communication (*Med. Sci.*, 1920, **2**, 285) the present authors reported that they had reproduced encephalitis lethargica in rabbits by intraocular inoculation, and that the virus could be continued by passage. In the present communication they report that they have been unable to reproduce the disease in rabbits by intraperitoneal, intravenous, or intratracheal inoculation. Intranasal inoculation by scarification followed by the application of a tampon infected with passage virus caused death with definite evidences of inflammation of the meninges. With regard to the infectivity of the organs of rabbits suffering from experimental encephalitis, the blood, bone marrow, lung, spleen, kidney, liver, and salivary glands were unable to propagate the disease to other animals. Interesting cross-experiments made in monkeys with the viruses of encephalitis and anterior poliomyelitis showed that after a primary subcutaneous inoculation of the virus of encephalitis, the animals succumbed, like controls, to a subsequent inoculation of the virus of poliomyelitis. Working with a virus obtained from a new case of encephalitis the results were not so certain as in the case of the virus previously studied. The authors infer that the virus of some cases of the disease is attenuated for the rabbit. W. B.

Marie, A. (de Villejuif), Levaditi, C., et **Banu, G.** Transmission expérimentale du tréponéma de la paralysie générale (Virus neurotrope) par contact sexuel. [**Experimental transmission of the treponema of general paralysis (neurotropic virus) by sexual contact.**] *Compt. rend. Acad. d. sc.*, 1920, **170**, 1021.

A strain of neurotropic virus, producing papulo-squamous lesions, has been used for these contact experiments. The virus can be transmitted from male to female and vice versa even within a short time from copulation (22 to 30 days). Whilst the infected female can be fecundated by a healthy buck, the male after infection seems to lose his power of fecundation partially or completely. A. D.

Meirowsky. Bericht der Salvarsankommission des Allgemeinen Aerztlichen Vereins in Köln. [**Report of the Salvarsan Commission of the General Medical Society of Cologne.**] *Münchcn. med. Wchnschr.*, 1920, **67**, 477.

As a result of a lecture by Meirowsky in 1918 in Cologne a Commission was appointed to study the injurious effects of salvarsan and its allies.

The Commission was under the presidency of Moritz and Zinsser with Meirowsky as secretary, and was composed of representatives from medicine, otology, ophthalmology, dermatology, neurology, and pathological anatomy. Erich Hoffmann was deputed to represent the German Dermatological Society. The report of the Commission is herewith presented in brief. Statistics from 182 doctors and clinics in Germany, Austria, Holland, and Denmark for a year comprise 13,000 injections of old salvarsan, 40,954 of sodium salvarsan, and 172,826 of neosalvarsan, a total of 225,780 injections.

As injurious sequelae special attention was directed to (1) fever of more than 3 days' duration ; (2) alimentary sequelae ; (3) cutaneous, renal, hepatic, ophthalmic, and nervous complications; (4) neuro-recurrences; (5) early tabes, paralysis, syphilis of the central nervous system; (6) deaths.

With regard to deaths the figures show that, following 225,780 injections of the types of drug specified, there were 20 fatalities, of which 12 were considered certainly, 5 doubtfully, and 3 indirectly due to the drug in question. The doubtful cases were those in which the injurious effects of mercury could not be excluded, and the indirect deaths included 2 cases of dermatitis and 1 of myelitis. Of the 12 undoubted and 3 indirect cases, 11 were considered to have been preventable and 4 as unavoidable, so that the chances of death where all precautions appear to be taken work out at 1 in 56,445 injections. Analysing the different types of drug shows, however, that there are considerable differences in the risk. In the old salvarsan series of 13,000 injections there were 2 deaths, one of which was due to overdosage (3 injections in 24 hours), leaving 1 case only in 13,000 injections.

The injections of sodium and of neosalvarsan were considered in two groups according as the dose was under 0·6 grm. or over this quantity. Of 39,701 injections of sodium salvarsan in doses less than 0·6 grm. there were 5 deaths, 3 being considered as undoubtedly due to the drug, whereas 2 were considered doubtful. One of the undoubted cases was considered preventable (dosage during dermatitis) leaving only 2 which apparently could not be foreseen—a proportion of 1 in 20,000 injections. The figures for doses above 0·6 grm. were too small to be of value, but there was 1 death in 1,253 such injections.

Of 162,792 injections of neosalvarsan in doses up to 0·6 grm. there were 3 certain, 2 doubtful, and 2 indirect fatal cases. The chance of death was 1 in 32,550 injections. A further analysis established the belief that only 1 death of the series was unpreventable, so that with neosalvarsan in doses not greater than 0·6 grm. there was 1 death in 162,792 injections. Of 9,035 injections of doses greater than 0·6 grm. there were 3 certain, 1 doubtful, and 1 indirect fatal issue—a proportion of 1 in 3,000 injections, this being 54 times as great as when the dose did not pass 0·6 grm. The greater number of deaths occurred in the treatment of primary and secondary cases, and the two sexes were equally affected. It was also determined that in about half of the fatal cases death ensued after the second or the third injection. With regard to the question of the relation of the total amount of drug injected to the fatal issue the figures showed that in doses up to a total of 1·0 grm. there were 3 deaths, with a total of 1·0 to 2·0 grm. 6 deaths, and with a total of 2·0 to 3·0 grm. there were 5 deaths. Apparently the first injections are particularly dangerous for the patient.

In 10 cases of the total of 20 fatalities death took place from encephalitis

(2 cases following salvarsan, 3 following sodium salvarsan, and 5 neosalvarsan, and of these 10 there were 6 that were certainly overdosed.

Five patients died from dermatitis and its complications following neosalvarsan. Two of these were probably mercuric in origin; all the others met their death from overdoses.

Of the 20 fatal cases 16 had also been treated with mercury, while 4 had received arsenical treatment alone. The Commission was strongly of opinion that as overdosage played an important part in causing death a maximum dose of 0·6 grm. for males and 0·45 grm. for females should not be exceeded.

With reference to jaundice there were 50 cases following 225,780 injections, and of these there were 43 in which there was a reasonable presumption that the arsenical drug was the sole cause, giving an incidence of 1 case of icterus in 5,260 injections. It was twice as frequent in males as in females. Jaundice occurring within 1 week after the last injection was regarded as early, and after the second week as late. Of the 50 cases 22 were early and 28 were late. Of the late series 2 occurred in 14 days, all the other after 1 to 9 and mostly 1 to 4 months. Jaundice occurred least frequently with neosalvarsan (1 : 6364), while with sodium salvarsan it occurred 1 : 2270 injections, and with old salvarsan 1 : 2100 injections. Early jaundice was seen most frequently with old salvarsan and sodium salvarsan, whereas the late form was seen especially in those treated with neosalvarsan for tertiary syphilis.

Injury to the skin occurred 48 times with 5 deaths. In 11 of these with 2 deaths mercury had also been freely exhibited in some form or other.

With reference to neuro-recurrences, there were 15 instances, of which 1 occurred with old salvarsan alone (1 : 13,000), 6 with sodium salvarsan and mercury (1 : 6,825), and 4 with silver-salvarsan. In 6 cases (2 males, 4 females) violent symptoms occurred on the part of the central nervous system, such as somnolence, vomiting, convulsions, suggesting a mild degree of encephalitis. All recovered. W. B.

Metalnikow, S. B. dysentérique et bactériophage de d'Herelle chez les chenilles de Galleria mellonella. [***B. dysenteriae*** **and d'Herelle's bacteriophage in the larvae of** ***Galleria mellonella.***] *Compt. rend. Soc. de biol.*, 1920, **83**, 667.

During many years Metalnikow has made extensive studies on experimental infections in the larvae of the beeswax moth, *Galleria mellonella.* He finds that this creature is very susceptible to living cultures of *B. dysenteriae*, Shiga, death occurring in 15–25 hours after the injection of $\frac{1}{80}$ c.c. of a Shiga emulsion. A wide dissemination of the microbe takes place, the body cavity becoming filled up with them. In the present study he has investigated the action of d'Herelle's bacteriophage (vide *Medical Science,* 1920, **2**, 182) in preventing the lethal effect of Shiga's bacillus. Doses of culture which killed the larvae within 24 hours had no effect if small quantities of the bacteriophage were injected 10 minutes previously. Even when the bacteriophage was injected half an hour after the dysentery culture the animals survived. An injection of bacteriophage $1\frac{1}{2}$ hours after the dysentery culture saved the lives of 2 out of 5 larvae, while an injection of dysentery 24 hours after a dose of bacteriophage killed all the animals in the series employed. On studying the mechanism of the destruction of dysentery bacilli by the bacteriophagic substance *in vivo* Metalnikow found that for 2 to 3 hours there was no apparent difference as compared with control animals inoculated with Shiga's bacillus only. After this time, however, a marked difference takes place in the two series. Instead of multiplying rapidly and continuously, the dysentery bacilli in the bacteriophagic series swell and become spherulated as in Pfeiffer's phenomenon. An intense phagocytosis ensues, the bacteria and their remnants are engulfed and rapidly digested. The author was able to make out a similar method of destruction in larvae actively immunized against *B. dysenteriae.*

W. B.

Fiessinger, N. L'immunisation antituberculeuse de la mite d'abeille. [**Anti-tuberculous immunization in the bee moth larva.**] *Compt. rend. Soc. de biol.*, 1920, **83**, 147.

Metalnikow, S. (1). Immunité de la chenille contre divers microbes. [**Immunity of larvae towards various bacteria.**] *Compt. rend. Soc. de biol.*, 1920, **83**, 119.

Metalnikow, S. (2). Sur la digestion des bacilles tuberculeux dans les corps des chenilles, des mites des abeilles (*Galleria mellonella*). [**On the digestion of tubercle bacilli in the larvae of *Galleria mellonella*.**] *Compt. rend. Soc. de biol.*, 1920, **83**, 214.

Hollande, A. Ch. (1). Remarque au sujet de la transformation en masse brunâtre des bacilles tuberculeux à l'intérieur des phagocytes du sang des chenilles. [**Note on the subject of the transformation of tubercle bacilli into a brown mass in the phagocytes of caterpillars.**] *Compt. rend. Soc. de biol.*, 1920, **83**, 670.

Hollande, A. Ch. (2). La formation du pigment brun-noir (mélanine) au cours de la phagocytose chez les insectes. [**Formation of melanin during phagocytosis in insects.**] *Compt. rend. Soc. de biol.*, 1920, **83**, 726.

Fiessinger confirms the older results of Metalnikow that tubercle bacilli introduced into the larvae of *Galleria mellonella* do not cause death. He finds no evidence for the view that the bacilli are actually killed, because even after a sojourn in the body of the larva for 8 hours they were still capable of killing guinea-pigs with ordinary tuberculosis. Metalnikow (1), on inoculating the larvae of *Galleria* with many different bacteria, shows that there are great differences in infectivity, so that three groups may be recognized. In the first of these, which includes tubercle bacilli of various types, *B. tetani, Trypanosoma brucei, Staphylococcus albus* and others, the larvae are highly immune. In a second group of infections comprising *V. cholerae, B. typhosus, Vibrion septique, B. welchii, B. anthracis,* the larvae succumb to large although they may be immune to small doses. A third group, comprising such microbes as *B. coli, V. metchnikovi, B. pyocyaneus, B. prodigiosus, B. subtilis, B. proteus,* causes death even in small doses. In the second communication Metalnikow confirms the statement of Fiessinger that in about 3 hours after injection of tubercle bacilli the phagocytes of *Galleria* show brownish masses which are the remains of the bacilli. Studying the same subject, Hollande considers that the brownish masses are not peculiar to the tubercle bacilli which have been phagocytosed, the pigment being the result of the action of enzymes on any substance which may be ingested. Thus it occurs after inoculation of *B. typhosus, M. gonorrhoeae,* as also with such substances as carmine, starch, talc, sodium carbonate, and various protein substances. Similar changes were also found with other larvae belonging to the genera *Vanessa, Agrotis, Arctia,* &c. The pigment is of the nature of melanin due to the action of a peroxydase of the leucocytes acting on a small quantity of blood plasma adherent to the bacteria at the moment of ingestion by the leucocytes. W. B.

Thjøtta, Th. (1). Om det saakaldte Neisser-Wechsberg'ske hæmningsfænomen i immunsera. [**On the so-called Neisser-Wechsberg inhibitory phenomenon in immune sera.**] *Norsk Mag. f. Lægevidensk.*, 1919, **80**, 897.

Thjøtta, Th. (2). **On the so-called Neisser-Wechsberg inhibiting phenomenon in bactericidal immune sera.** *J. Immunol.*, 1920, **5**, 1.

Apart from trivial differences, the second of these papers is a literal translation in English of the original, which was published in Norwegian, and they constitute an important addition to our knowledge of the paradoxical phenomenon to which Neisser and Wechsberg drew attention almost 20 years ago under the name 'Complementablenkung'. They showed that whereas small or medium doses of bactericidal sera exhibited their bactericidal function with the homologous strain of the microbe, larger doses of the same serum were without effect. They also showed that the dose of complement-bearing serum which sufficed to activate a certain dose of inactivated serum was not capable of doing so when larger doses of immune serum were added. The explanation offered by Neisser and Wechsberg was that the surplus of amboceptor in the immune serum brought about the inhibition of the bactericidal action because this surplus united with complement and rendered the effective utilization of the latter impossible. Other theories have been proposed by Levaditi, Gay, Sormani, and others, but the view of Neisser and Wechsberg has been the one generally accepted. In a long series of clearly thought out experiments made with an exact technique, Thjøtta shows in the first place that the Neisser-Wechsberg reaction is specific. It occurs both in active and inactive sera, and it develops during immunization. In active sera, from immunized animals, examined without the addition of foreign complement, the phenomenon presents itself as a complete abolition of the normal bactericidal action. Thjøtta points out that although the inhibiting action, as well as the bactericidal action, result from immunization, it does not follow that both these functions are exercised by the same antibody—the bactericidal amboceptor—as was supposed by Neisser and Wechsberg. If, as the author points out, the bactericidal titre (B) is taken as an indication of the amount of amboceptor present, this and the inhibiting dose (I) should stand in some direct proportion to each other if the two functions were carried out by the same antibody. His experiments indeed show that this is not so. Thus the bactericidal titres were found to vary in their proportion to the inhibiting titre (taken as 1) from 0·06 to 0·0000078. He believes that the inhibiting bodies differ from agglutinins, lysins, or precipitins, and must be regarded as specific antibodies which combine with dissolved antigen to form complexes which have a marked tendency to absorb complement and withdraw it from bactericidal antibodies. Experiments clearly show that the titre of the inhibition varies according to the dose of complement. With a small dose of the latter smaller doses of inhibiting antibodies can be demonstrated than with a larger dose of complement. The inhibiting antibodies do not actually affect the bacteria themselves nor can they be removed from serum by absorption with an emulsion of the homologous bacteria. Thjøtta also shows that inhibiting bodies may be present in sera that lack any bactericidal power. The facts that there is no relation between the bactericidal and the inhibiting titre, that sera may have a high bactericidal and no inhibiting titre, and that inhibition can still be found in sera from which bactericidal amboceptors have been removed by homologous antigen, render Neisser's theory untenable in the opinion of the author. On the other hand, Thjøtta's own view that inhibition is due to a specific antibody which in the presence of dissolved antigen absorbs complement with great avidity, seems borne out by the fact that the titre of inhibition varies with the dose of complement, since a certain dose of inhibiting body must absorb a certain amount of complement. If the dose of the latter is larger than required the remainder of the complement can be used by the bactericidal substances. It is also borne out by the fact that if the dose of complement is very small the existence of inhibiting antibodies can still be demonstrated, and that bacteria which have been in contact with inhibiting serum can be entirely vulnerable in a non-inhibiting serum.

The specific inhibiting antibody acts in the manner of an anti-complement in that it hinders the function of the complement. It is, however, no ordinary anti-complement, since it can only act in the presence of the homologous antigen, the supposition being that it is a combination of the antigen and the inhibiting antibody which absorbs the complement. The inhibiting antibody must be classed as an amboceptor, but not of the kind that enters into union with solid bacterial proteins, because it cannot be removed by absorption and centrifugalization or filtration. Thjøtta's long and interesting paper should be studied in the original which contains many interesting facts other than those dealt with in this short abstract. In particular his technique is recommended for further investigations.

W. B.

Fürst, Th. Ueber Steigerung der Antikörperproduktion durch unspezifische Reizwirkung intravenöser Methylenblauinjektion. [**On increase in antibody production by means of non-specific action of intravenous injections of methylene blue.**] *Arch. f. Hyg.*, 1920, **89**, 161.

Experiments to show that the agglutination titre of serum of animals immunized with paratyphoid bacilli can be increased, without further injection of the homologous bacilli, if the animal is injected with 2 c.c. of a 0·5 per cent. solution of methylene blue. Blood counts showed that contrary to the leucocytosis produced by protein substances methylene blue induces a leucopenia especially of the polynuclear types. The highest titre of the antibody curve was obtained when the leucopenia was at its nadir. The author considers that it is probably a toxic property of the methylene blue which sets the antibodies free in the serum. W. B.

Dale, H. H. Conditions which are conducive to the production of shock by histamin. *Brit. J. Exper. Path.*, 1920, **1**, 103.

When, during the war, research was being carried out into the cause of the shock which was found to follow extensive injury, the author called attention to a similar condition which can be induced in animals by the injection of histamin. The relation of this shock to wound shock 'can only be regarded as an open possibility'.

Histamin can be given to a normal cat, not under an anaesthetic, in doses up to 10 mgm. per kilo, without severe or lasting effect. In the same animal, at the end of anaesthesia with ether, 1 to 2 mgm. per kilo will produce the characteristic shock. Anaesthesia with nitrous oxide has not this effect. A large haemorrhage greatly reduces the resistance to histamin.

On the day following the removal of the suprarenal glands the resistance of cats to histamin was greatly lowered, as little as 0·16 mgm. per kilo, given without an anaesthetic, proved fatal.

The circulatory condition developing in the 24 hours following removal of the suprarenal glands has features in common with that produced by histamin, including a pronounced increase in the proportion of corpuscles in the blood. P. F.

Baumgärtel, Tr. Wassermannsche und Sachs-Georgische Reaktion bei Syphilis. [**The Wassermann and Sachs-Georgi reaction in syphilis.**] *München. med. Wchnschr.*, 1920, **67**, 421.

The author has taken the trouble to analyse in tabular form the published results of the comparison between the Wassermann and the Sachs-Georgi reactions in over 25,000 cases of which he has himself contributed 7,000 cases. From a study of the results he concludes that the two reactions agree in about 90 per cent. He recommends that the test should be carried out at 37° C., and the results should be read in 2, 24, and 48 hours. A very complete set of references to the literature on the subject accompanies the paper. W. B.

Besredka, A. De l'action des sérums par la voie respiratoire. [**On the action of sera administered by the respiratory tract.**] *Ann. de l'Inst. Pasteur*, 1920, **34**, 51.

The introduction of serum through the respiratory tract is innocuous, but if the animal is previously sensitized, $\frac{1}{10}$th or $\frac{1}{15}$th of a c.c. injected into the trachea suffices to produce anaphylactic shock. The anaphylactic shock varies according to the density of the serum: viz., the higher the density of the serum the lower the shock, and in practice 10 or 15 times the amount of serum can be administered. The respiratory tract absorbs antibodies. In fact, by inhalation of tetanic and diphtheritic antitoxins, the animal is protected against a lethal dose. A. D.

Iyengar, K. R. K. Frequency of a positive Wassermann reaction in an unselected adult male Indian population. Significance and value of a positive Wassermann reaction in leprosy. *Indian J. M. Research*, 1919, **7**, 398 and 407.

In the first of these two papers the author tested an unselected collection of Indian natives, who came to the Pasteur Institute, Kasauli, for antirabic treatment. They numbered 400, and were of all ages between 20 and 60. The antirabic treatment itself was shown to have no effect upon the Wassermann reaction. 22 per cent. gave positive results with one of the techniques approved by the Medical Research Council. In the second paper the author examined 100 cases of leprosy, and of these 41 per cent. gave a positive reaction. The greatest incidence was in the nodular

type. Since the 400 men in the first paper were not leprous, the author confirms the view that a positive reaction can be due to leprosy alone.
P. F.

Fabry, P. Sur l'agglutinabilité des microbes atténués. [**On the agglutinability of attenuated microbes.**] *Compt. rend. Soc. de biol.*, 1920, **83**, 164.

The typhoid bacillus is cultivated in broth with increasing doses of 5 per cent. phenol. When subsequently cultivated in plain agar, it is found to have acquired the property of being agglutinated at higher dilutions than the strain which has never been in contact with the disinfectant.
A. D.

Cruickshank, J. The value and mechanism of the colloidal gold test. *Brit. J. Exper. Path.*, 1920, **1**, 71.

The difficulty in applying Lange's colloidal gold test to the cerebrospinal fluid has been in the preparation of suitable samples of colloidal gold. The author describes fully the technique. A complete review of the literature of the reaction follows. The author's practical test of the method upon a number of cases confirms the results of other workers. It is valuable in the diagnosis of general paralysis, but there is no parallelism between it and other tests. The substance in the spinal fluid of paretics which causes precipitation of colloidal gold is not dialysable, and resides in the globulin fraction of the protein, and in this respect resembles the Wassermann reacting substance. It is not altered by heating to the coagulation point of protein. The reaction is not due to peptone. The various types of reactions can be simulated by mixtures of globulin and albumin, the globulin acting as a precipitating agent and the albumin as an inhibitory or protective one. 'Luetic' reactions are due to an amount of albumin sufficient to obscure partially the precipitating effect of the globulin. As the globulins obtained from negative spinal fluids, even when used in concentrated form, are almost inactive, the precipitating action of paretic fluids cannot be ascribed solely to the increase in globulin, but it is probably dependent on a specific alteration of the physical state of the globulin, which is associated with a positive electric charge. Human serum globulin has, also, the characters of a positive colloid, but the 'paretic' and 'luetic' reactions of spinal fluid cannot be attributed merely to the passage of serum globulin into the spinal fluid. The 'meningitic' reactions, on the other hand, may be due to the leakage of plasma through damaged meninges. The author is of opinion that, for the present, only reactions of the 'paretic' or 'luetic' types should be regarded as of real diagnostic value, and that the 'meningitic' reactions should be held *sub judice*. P. F.

Drew, A. H. The comparative oxygen avidity of normal and malignant cells measured by their reducing powers on methylene blue. *Brit. J. Exper. Path.*, 1920, **1**, 115.

The author measured the oxygen avidity of normal and malignant tissues by estimating the quantity of methylene blue reduced by each. In the case of normal tissues, kidney, testis, brain, &c., decolorization of the blue proceeds at once, but with sundry tumours from mouse or man there is a long initial period during which no decolorization takes place, and the decolorization is never so active as with normal tissues. If normal tissue is washed with a soluble calcium salt, its reducing power is converted to the tumour type, but it regains its original behaviour on being treated with sodium salts. Decolorization is dependent upon the integrity of the cell, it is absent when the tissue is ground up. It was found that the lag observed in the case of tumours could be abolished by washing all oxygen out of the solvents with hydrogen, the small requirements of the tumours in oxygen being met by the dissolved oxygen. Thus the oxygen demands of normal tissues are much greater than those of tumour tissues.

P. F.

Tunnicliff, Ruth. The action of leucocytic extracts on the phagocytic activity of leucocytes. *J. Infect. Dis.*, 1920, **26**, 447.

The action of leucocytic extracts has been extensively studied by Pettersson, Hiss and Zinsser, and others. The present authoress has confined herself to the investigation of the changes which leucocytic extracts produce on phagocytic activity. She finds that when leucocytic extracts from the horse or dog are injected into rabbits a definite leucocytosis is obtained, reaching a maximum in about 6 hours. Using pneumococci and *Streptococcus viridans* as test objects she found that the phagocytic activity of the leucocytes, set free into the circulation by the extract, was greater than when the leucocytes of control animals were used. Leucocytic extracts appeared to have no influence in counteracting the leucopenia which follows injections of benzene. W. B.

Weinberg et **Nasta.** Rôles des hémolysines dans l'intoxication microbienne et propriétés thérapeutiques des sérums normaux. [**Rôle of haemolysins in microbic intoxications and the therapeutic properties of normal sera.**] *Compt. rend. Acad. d. sc.*, 1920, **170**, 101.

The injection of *B. perfringens* in sublethal doses in guinea-pigs produces at first haemoglobinuria and afterwards haematuria. The toxin of *B. perfringens*, freed of its haemolysin by contact with blood corpuscles, injected in guinea-pigs is harmless. The importance of the haemolysin is so great that the curative action of the antitoxic serum is proportional to its antihaemolytic action. Normal horse serum neutralizes the haemolysins of *B. perfringens* and also that of *Vibrion septique*. In regard to staphylotoxin the administration of horse serum only retards the death of the animal, and in the case of streptolysin the horse serum has no action whatever. The curative properties of normal serum in certain diseases is due therefore to its antihaemolytic power. A. D.

Nicolle, Ch. et **Conseil, E.** La virulence du sang des rougeoleux n'est pas contestable. [**The virulence of the blood of patients affected with measles is incontestable.**] *Compt. rend. Soc. de biol.*, 1920, **83**, 56.

The inoculation of 8 c.c. of measles blood 12 hours after the apparition of the rash produced in a monkey on the tenth day an elevation of temperature going from 40·2 to 40·7°C. Two monkeys were inoculated into the peritoneal cavity with 4 c.c. each of blood from the infected one and 1 c.c. of the blood of this same animal was injected subcutaneously to a healthy child. The latter gave the classical evolution of measles. From this child another passage was made into three monkeys with positive results in two and negative in the third, which was a young one. A. D.

Albanese, A. Ricerche sulla presenza di fermenti preformati nel sero di sangue, per le proteine delle fibre nervose di animali della stessa specie e di specie diversa di quella cui appartiene il sero. [**Preformed ferments of the blood.**] *Arch. Ital. di Chir.*, 1920, **1**, 711.

Merzbacher showed (*Neurolog. Centralbl.* 1905, No. 4. **24**, 150) that nerves which had been transplanted into animals of the same species underwent regressive changes, while those transplanted into animals of a different species rapidly necrosed and the organism reacted towards them as towards foreign bodies. Alexis Thomson (*Edinburgh Med. J.*, March 1917) put forward the hypothesis that anaphylactic and biochemical phenomena played a part in the changes observed in transplanted tissues, the phenomena depending on the production of special ferments induced by the presence of the foreign tissue in the organism. Albanese has conducted a series of experiments proving the existence of preformed ferments in the blood, ferments, that is, which exist independently of the introduction of a foreign protein into the blood and are without the specific action which characterizes those arising from the introduction of heterogeneous protein into the organism.

For demonstrating the activity of the ferments Albanese employed the method proposed by Abderhalden; a portion of nerve, cut into fragments and repeatedly boiled in order to remove every trace of blood, was placed in a small membranous sac together with a small quantity of the serum to be tested; the sac immersed in sterilized distilled water was then placed in the warm chamber at 37° C. After 16 hours the water was tested for the presence of the products of protein digestion. The experiments show distinctly: (1) That the serum of the guinea-pig is without action on the nervous and muscular tissues of the same or of a different guinea-pig; while those tissues from the dog are acted upon powerfully. (2) That the serum of the rabbit has a powerful action on the nerve-tissue of the dog. (3) That the serum of the rabbit has an action on the nerve-tissue of the guinea-pig, well marked but less powerful than on the nerve-tissue of the dog. (4) That the serum of the guinea-pig has a well-marked action on the nerve-tissue of the rabbit, but less powerful than on the nerve-tissue of the dog. (5) That the serum of the dog acts on the nerve-tissue of the guinea-pig and rabbit.

In addition to demonstrating the presence of preformed proteolytic ferments in the blood, these experiments go to show that the action of such ferments is the more energetic the less the degree of affinity between the animals experimented on. T. W. P. L.

Cook, Marjorie W. The relation of the rate of absorption of antigen to the production of immunity. *J. Immunol.*, 1920, **5**, 39.

A number of workers, among them Doerr and Pick, have established the fact that the rate of antigen absorption in sensitized and immunized animals is quicker than that which obtains in animals not previously treated. The present authoress has attempted to find out whether the process of immunity production is in any way dependent on the altered absorptive powers of the animal organism. In order to cause alterations in the permeability of the cells she considered that an excess of sodium-ions or of calcium-ions into the blood might reveal the change better than in the cases where the antigen alone was used. The increased permeability of the cells by sodium-ions and the decreased permeability by calcium-ions have already been investigated by Loeb, Osterhout, and others. Using egg albumen as the antigen the authoress found that when Na- or Ca-ions were given in addition, the results were different from those obtained in control animals, for the precipitins appeared more rapidly and in much higher concentrations in rabbits treated with sodium citrate. The reverse was true when calcium chloride was employed. The determination of the degree of leucocytosis did not indicate that it was an important factor in bringing about changes in immunity production. These results occurred not only with precipitins, but also with agglutinins and opsonins. W. B.

Thomsen, Oluf. Méthode de dénombrement direct des plaquettes sanguines. [**Method of enumerating the blood-platelets.**] *Compt. rend. Soc. de biol.*, 1920, **83**, 505.

The author considers the methods, now in use for the counting of blood-platelets, both complicated and inexact. He has devised a new method based on their stability when held in suspension in plasma. His technique is as follows: The blood (4·5 c.c.) is obtained by venepuncture, and run into a graduated tube containing 0·5 c.c. of a 10 per cent. solution of sodium citrate. The tube is closed with a stopper, inverted several times to ensure efficient mixture with the citrate of sodium, and then left for 2 to 3 hours to enable the red corpuscles to fall to the bottom. A small quantity of this citrated plasma is drawn off with a pipette and suitably diluted with physiological saline. The degree of dilution depends on the number of platelets present; the general rule being to dilute so that the resulting volume is from 2 to 4 times greater than that of the plasma taken. A drop of this mixture is then placed in a Thoma-Zeiss haemocytometer, and the platelets counted, using objective *D*, ocular Zeiss 4. Suppose A is the average number of platelets counted per cubic millimetre, then the corrected number is $A \times 4{,}000 \times$ coefficient of dilution. The 4,000 is the usual factor to allow for the dimensions of the Thoma-Zeiss apparatus—$\frac{1}{20}$ mm. wide, $\frac{1}{20}$ mm. long, $\frac{1}{10}$ mm. deep, i. e. a volume of 1/4000 c.mm. But allowance has to be made for the depth of the layer of red corpuscles. 5 per cent. of this is taken to represent fluid. Let a be the total volume (in c.c.) of the mixture, and b that of the bottom layer of red corpuscles. Acting on the assumption that the number of platelets per c.mm. = total number present divided by total volume of blood taken we have the following expressions:

Total volume of citrated plasma $= (a + 0{\cdot}05\, b)\, 1000$ c.mm.
Total volume of blood taken $= (a + b - 0{\cdot}5)\, 1000$ c.mm.

If now $A' = A \times$ coefficient of dilution, the above may be expressed as a formula thus:

$$X = \text{Number of platelets per c.mm.} = \frac{A'\, 4{,}000 \times \left(a + \dfrac{5b}{100}\right) 1{,}000}{(a + b - 0{\cdot}5)\, 1{,}000}.$$

It is to be noted that this does not agree with the formula as given by the author, who writes $X = \dfrac{A' 4{,}000 \left(a + \dfrac{5b}{100}\right) 1{,}000}{(a + b : 0{\cdot}5)\, 1{,}000}.$

In the event of the worker possessing no centrifugalizer, an empirical table of values is appended showing a factor by which A' may be multiplied in order to determine X. But this requires a previous determination of the number of red corpuscles per c.mm., on which the above-mentioned factor depends. The author says that agglutination has not been observed.

With regard to a possible fall of platelets gradually vitiating the count, he remarks there is no visible difference after an interval of 6 hours. It is found that the platelet count varies between the extremes 206,700 and 413,400 per c.mm., the general average being 250,000 to 300,000 per c.mm. The method is such that the blood so drawn from the patient may be used for various other clinical purposes, such as the counting of the red and white cells, and the Wassermann reaction, &c. It seems fair to point out that some revision of the text of the paper is desirable, there being several slips, the rectification of which wastes much time. The author does not show any steps by which he deduces his formula, and we disagree with the denominator. W. A. M. S.

Gram, H. C. Les hématoblastes dans l'anémie pernicieuse. [**Blood-platelets in pernicious anaemia.**] *Compt. rend. Soc. de biol.*, 1920, **83**, 714.

The method of Oluf Thomsen for counting the blood-platelets, with a slight modification in technique, has been employed by H. C. Gram in cases of pernicious and aplastic anaemia. In normal individuals the number varies between 300,000 and 550,000 per cubic millimetre, but the variations in any particular individual are much more limited. In certain infections and diseases of the blood, the number is greatly reduced, especially in influenza, typhoid fever, purpura, and lymphatic leucaemia.

In a first examination of 24 cases of pernicious anaemia, the results were: 1 case with 201,000 to 250,000 platelets per c.mm., 2 with 151.000 to 200,000, 5 with 101,000 to 150,000, 6 with 51,000 to 100,000, and 10 with 4,000 to 5,000. A haemorrhagic diathesis began to appear when the number fell below 200,000, and it was always produced when the number became 100,000. If the condition improved the number of platelets rose to the normal, 500,000 per c.mm. When the anaemia got worse the number of platelets fell as the haemorrhagic symptoms showed themselves afresh

As regards technique, the author prefers, after sedimentation of the citrated blood, to dilute the plasma twenty times with 0·9 per cent. sodium chloride. His formula is $Ps = Pp \times (Vsc + Vg) / Vsc + Vc$, where Ps is the number of platelets per c.mm. of blood, Pp is the number of platelets per c.mm. of citrated plasma, Vsc the volume of citrated blood (5 c.c.), Vg the volume of the red corpuscles, and Vc the volume of citrate used (0·5 c.c.). The absolute volume of the red corpuscles may be determined by centrifugalization. It may also be found by determination of the haemoglobin as he shows. Thomsen's table of constants mentioned in the above paper can only be used for normal individuals. W. A. M. S.

Shunk, I. V. A modification of Loeffler's flagella stain. *J. Bact.*, 1920, **5**, 181.

The modification consists chiefly in the use of a solution of anilin oil in alcohol (1 : 4) in connexion with a ferric chloride tannic acid mordant.

The stain recommended is Loeffler's methylene blue to which is added $\frac{1}{10}$th of its bulk of anilin oil in alcohol (1 : 4). All the usual precautions for staining cilia have to be carried out. When the films have dried in air they are treated with 2 solutions in the cold.

Solution A.	Ferric chloride 1 : 20 aqueous sol.	1 part
	Sat. aqueous sol. of tannic acid	3 „
Solution B.	Anilin oil	1 „
	95 per cent. alcohol	4 „

In practice about 8 drops of sol. A are placed on the cover-glass and this followed immediately by a drop of sol. B, the combination being allowed to act at room temperature for 2 minutes, then washed off with water. The cover-glass is then flooded with Loeffler's blue containing as stated $\frac{1}{10}$th of its bulk of anilin oil alcohol (sol. B). The stain is allowed to act for 2 to 3 minutes at room temperature, the cover-slip being then washed thoroughly and allowed to dry.

The chief advantages claimed for the method are: (1) its simplicity, (2) the use of solutions that keep well, (3) the use of all solutions at room temperature, (4) the high percentage of successful results even in the hands of the inexperienced. W. B.

Breinl, F. Ueber das Verhalten gram-positiver und gram-negativer Bakterien zu den Halogenen. [**On the behaviour of Gram-positive and Gram-negative bacteria in the presence of the halogens.**] *Ztschr. f. Immunitätsforsch. u. exper. Therap.*, 1920, Orig. **29**, 343.

It is already known, through the researches of Eisenberg, and others that the inhibiting and sterilizing effects of certain anilin colours are much greater on Gram-positive than on Gram-negative bacteria. The present author has continued work of this kind with special reference to the difference in action, of halogens, on the two kinds of bacteria. It was found that watery solutions of iodine, bromine, or chlorine are three to six times more effective on Gram-positive than on Gram-negative bacteria. The Gram-negative bacteria adsorb the halogens much more completely than the Gram-positive. W. B.

Zeug, Max. Äquilibrierte Salzlösungen als indifferente Suspensionsflüssigkeiten für Bakterien. [**Balanced salt solutions as indifferent fluids for bacteria.**] *Arch. f. Hyg.*, 1920, **89**, 175.

Bacteriologists have usually used a 0·85 per cent. common salt solution for the preparation of bacterial emulsions, and it has generally been considered that this menstruum is an indifferent one. The deleterious effect, however, of this solution has been emphasized by more than one worker, and this is confirmed by the present author, who states that several micro-organisms, notably *V. Metchnikovi*, are rapidly killed off when suspended in salt solution. He finds that a balanced solution for this vibrio must contain sodium chloride 0·5 per cent., potassium chloride 0·5 per cent., magnesium chloride 0·1 per cent., and calcium lactate 0·5 per cent. For staphylococcus and proteus, solutions of inorganic salts alone will suffice if they consist of NaCl, KCl, $CaCl_2$, and $MgCl_2$. For staphylococcus, the best solution was one composed of NaCl 0·5 per cent., potassium chloride 0·5 per cent., calcium chloride 0·1 per cent., and magnesium chloride 0·5 per cent. All water used should be doubly distilled from glass. W. B.

BIOCHEMISTRY

Cullen, G. E. and **Van Slyke, D. D.** **Determination of the fibrin, globulin, albumin, and nitrogen of blood plasma.** *J. Biol. Chem.*, 1920, **41**, 587.

The description of a method for the separation of the fibrin, globulin, and albumin of blood plasma so that they can be estimated by the Kjeldahl method. R. A. P.

Thies, Ruth C., and **Bagg, H. J.** **The effect of intravenous injections of active deposit of radium on metabolism in the dog.** *J. Biol. Chem.*, 1920, **41**, 525.

Berg and Walker concluded from some experiments upon dogs that the ingestion of small quantities of radium salts was followed by a stimulation of the break-down processes of the body. The output of nitrogen in the urine was increased and there was a slightly larger volume of urine excreted. The present experiments deal with the administration of radium emanation intravenously. The doses employed showed a cumulative effect, leading in two dogs to nausea and refusal of food as well as general indisposition. In every case the injection of the active deposit was followed by an increased output of nitrogen in the urine, reaching its maximum on the second day after the injection. An interesting point appeared in the creatinin excretion of one of the dogs. Creatinin excretion is of course usually constant in the urine, even when the other nitrogen constituents are varied within wide limits. In this dog the administration of the radium emanation produced a marked increase in creatinin elimination. This was not a question of fever as the changes in creatinin elimination did not coincide with the temperature changes. R. A. P.

Van Slyke, D. D. and **Palmer, W. W.** **Studies of acidosis. XVI. The titration of organic acids in urine.** *J. Biol. Chem.*, 1920, **41**, 567.

Apart from his other contributions, we shall always feel grateful to Van Slyke and his associates for the number of simple and valuable technical methods introduced by them. Another method has appeared which promises to replace, in part, the clinical estimation of acetone bodies in the urine by a comparatively simple titration. The method is based upon an ingenious use of the dissociation constants of the acids titrated. Put briefly, in the presence of the salt of a weak acid such as an organic acid, a larger amount of an acid such as hydrochloric acid is needed to produce a given change in the reaction of a fluid. So if the titration is always performed between exactly the same limits of reaction, the limits being defined so that the stronger acids are not titrated, the titration figure will measure the weak acids only. The only mineral acids found in urine in sufficient quantity to affect the titration are the weak acids carbonic and phosphoric. These are removed before the estimation by precipitation with calcium hydroxide. Weak bases would also of course affect the estimation. Ammonia is titrated to the extent of about 5 per cent., but this is not a significant error, especially as the ammonium salts of the organic acids titrate more completely. Creatinin is titrated almost quantitatively by the method, and creatin if present to the extent of 60 per cent. A correction can be applied for the error introduced in this way. Apart from this the presence of amino acids would be a disturbing factor. In ordinary urine the amount is insignificant. Urea is without effect upon the titration.

A description of the method will indicate its simplicity. '100 c.c. of urine measured roughly, are thoroughly mixed with 2 grm. of finely powdered calcium hydroxide, allowed to stand about 15 minutes with occasional stirring, and then passed through a dry folded filter (this treatment removes the carbonates and phosphates). To 25 c.c. of the filtrate in a 125 c.c.–150 c.c. test tube of clear glass is added 0·5 c.c. of 1 per cent. phenolphthalein solution, and 0·2 N HCl from a burette, until the pink colour just disappears. 5·0 c.c. of 0·02 per cent. tropeolin 00 solution are then added. As the indicator solution is added it is thoroughly mixed with the urine by shaking the tube, to avoid possible precipitation of the tropeolin 00. Finally 0·2 N HCl is added from the burette until the red colour equals that of a standard solution containing 0·6 c.c. of 0·2 N HCl, 5 c.c. of tropeolin 00 solution, and water to a total volume of 60 c.c. When the end point is approached, sufficient water is added to the titrated solution to make its volume equal to that of the 60 c.c. standard solution used in a similar tube as a colour control.'

The average 24-hour excretion of organic acid for healthy men was found to be per kilo of body weight 8·2 c.c. of 0·1 N acid uncorrected for creatinin or 6 c.c. corrected for creatinin, the extreme range for the normal was 5·7 to 9·8 c.c. uncorrected. Day and night periods were approximately the same. The paper further contains an account of two cases: the one, a case of methyl alcohol poisoning, gave an organic acidosis which could only be accounted for, in part, by the excretion of known acids. The other, a case of diabetes which went on to coma, gave an organic acidosis which was an accurate parallel to the rise in the excretion of acetone bodies in the urine. This parallelism was so close that it indicates the probabilities (1) that organic acids other than the acetone bodies are not excreted in significant amounts in diabetic acidosis, and (2) that the easily preformed organic acid titration may be used for approximate estimation of the acetone bodies in diabetic urine.

R. A. P.

Short, J. J. The formation of acetone bodies following ether anaesthesia and their relation to the plasma bicarbonate. *J. Biol. Chem.*, 1920, **41**, 503.

After ether anaesthesia, the urine of a patient is often found to give a positive test for acetone bodies with ferric chloride and sodium nitroprusside. This has led to a belief that the diminished alkaline reserve also found after ether anaesthesia is accounted for by the presence of the acetone bodies. In support of this, Reimann and Bloom claimed that 60 per cent. of the fall in blood bicarbonate was to be attributed to the blood acetone bodies. The author thinks that possibly the results obtained by Reimann and Bloom were due to a faulty technique in the estimation of the acetone bodies introduced by the ether. He examined a series of blood and urine specimens for acetone and hydroxybutyric acid before and after ether anaesthesia, as well as performing estimations of the blood bicarbonate. During the period of anaesthesia, averaging 40 minutes, the CO_2 combining power of the blood diminished. This was, however, not correlated with an increase in the concentration of acetone bodies in the blood. In two cases examined for some time after the anaesthesia, these bodies increased a few hours later, and were excreted in the urine. During the appearance of the β-hydroxybutyric acid in the blood, the CO_2 combining power even increased. It appears, therefore, that we have to look to some other source for the decrease in the alkaline reserve. R. A. P.

Bayliss, W. M. The action of gum acacia on the circulation. *J. Pharmacol. and Exper. Therap.*, 1920, **15**, 29.

Bayliss criticizes the work of Hanzlik and Weidenthal[1] because of the wide variations in coagulation time obtained by them. He suggests that their results are incorrect and that their conclusions are unwarranted.

H. E. R.

Fenger, F. Comments on the clotting efficiency of thromboplastic agents. *J. Pharmacol. and Exper. Therap.*, 1920, **15**, 167.

Decrease in effective blood-volume, whether as the result of haemorrhage or by stagnation in capillary areas, requires additional fluid in the blood-vessels. Saline is not efficient as it escapes rapidly through the capillary wall. The alternative is blood transfusion or the use of gum-saline. Gum-saline (6–7 per cent. gum acacia in 0·9 per cent. sodium chloride) is more easily obtained and it can be kept indefinitely ready for use. Its efficacy is due to its effect as a colloid in producing an effective osmotic pressure—that is, it retains water in the blood-vessels because it does not pass through the capillary wall, and it has an osmotic attraction for water. It has no drug-like action, does not produce haemolysis or anaphylaxis. It may be useful in wound shock or to combat toxic escape of fluid from the blood-vessels. Neither blood transfusion nor gum-saline have any permanent effect when vasomotor control is lost. Gum acacia is recommended for the perfusion of excised organs as it diminishes oedema. H. E. R.

Luckhardt, A. B., Koch, F. C., Schroeder, W. F., and Weiland, A. H. The physiological action of the fumes of iodine. *J. Pharmacol. and Exper. Therap.*, 1920, **15**, 1.

The research was carried out in order to study the absorption of iodine from the skin and lung surfaces. Iodine, in the form of tincture, painted on the skin of man, does not appear in the urine within two hours, but within twenty-four to thirty hours appreciable quantities are excreted. When applied in the form of fumes less is absorbed, probably because a smaller dose remains on the skin. Experiments on dogs show that the iodine content of the thyroid gland is increased, and that in some cases the histological appearance is altered. Iodine fumes are absorbed from the lungs and the element appears in the urine. Intratracheal inhalation causes dyspnoea and cough. At first there is a slight rise in blood-pressure, with an increased rate of respiration and a quickened heart-beat; this is followed by decrease in the rate of the heart-beat and a fall in blood-pressure. Death is due to respiratory failure. Respiratory affections (onset of distemper in dogs) hasten death. The minimal fatal dose was 14 mgm. per kilo. The danger of iodine inhalations, especially in respiratory affections, is pointed out. H. E. R.

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[1] *Medical Science*, 1920, 2, 92.

Wetzel, N. C. and **Sollmann, T. Iodine absorption from the human skin.** *J. Pharmacol. and Exper. Therap.*, 1920, **15**, 169.

In contrast with the above it was found that iodine does not appear in the urine after it has been painted on the skin. H. E. R.

Plötz, W. Vergleichende Untersuchungen über die hämolytische Wirkung einiger Chlorderivate des Methans, Äthans und Äthylens. [**Comparative experiments on the haemolytic effect of some chlorine derivations of methane, ethane, and ethylene.**] *Biochem. Ztschr.*, 1920, **103**, 243.

The haemolytic effect of some substances, chlorine derivatives of methane, ethane, and ethylene have been tested, using guinea-pig and ox blood for the purpose. An average of the results shows that increasing molecular weight, due to the entrance of the chlorine atom, increases the haemolytic power, for instance, upon an arbitrary scale—

CH_2Cl_2	0·42	$CH_2Cl\ CH_2Cl$	0·52
$CHCl_3$ (chloroform)	1·0	CH_3CHCl_2	0·95
CCl_4	10·5	$C_2H_2Cl_4$	6.

The author was unable to confirm the Traube theory of the action of narcotics, that the action of narcotics is correlated with their power of altering the surface energy of the cell surface. R. A. P.

Ide. Nature of the constituents of gland extracts used in therapy ('opotherapy'). *Bull. Acad. roy. de méd. de Belg.*, 1919, **29**, 1287. (*Chem. Abst.*, 1920, **14**, 1845.)

The active substances, or hormones, cannot be protein in nature since they are non-specific, are easily diffusible, arising as they do in one organ and exhibiting their action on another, and are not easily destroyed in the digestive process. They are, therefore, considered to be relatively simple crystalloids which should be soluble in water, and easily purifiable by dialysis or by precipitation of the accompanying proteins. The use of dried glands is unnecessary, and a plea is made to the chemists to apply the methods used in the isolation of the active principles in plants to the production of pure concentrated hormone preparations. C. G. L. W.

Cohn, A. E., and **Levy, R. L. A comparison of the action in patients of γ. strophanthin and digitalis.** *Proc. Soc. Exper. Biol. and Med.*, 1920, **17**, 81.

The two drugs were given in standardized amounts to patients suffering from fibrillation of the auricles. The speed of action of strophanthin is greater than digitalis, though when strophanthin is given in divided doses it may take two hours to get an effect. With digitalis the effect on the rate of the ventricle outlasts that of strophanthin. It is rare for strophanthin to keep the rate low for more than five days, while the retardation with digitalis has been observed for as long as twenty-three days. C. G. L. W.

Davenport, C. B. **Heredity in twin births.** *Proc. Soc. Exper. Biol. and Med.*, 1920, **17**, 75.

It is probable that certain strains of humans have a special tendency to the production of twins. The quality is not entirely maternal, as has been asserted. Twins are of two types, those derived from a double ovulation and those produced by a single ovulation with a subsequent fission or budding of the fertilized egg. Such single egg twins are easily distinguished by being enveloped in the same chorion. They are always of the same sex. Interesting facts are given regarding the influence of the paternal parent on the frequency of twinning. This influence is concerned with the capacity of the male to fertilize all of the eggs ovulated with sperm which contains no lethal factors. Both the capacity for complete fertilization (high fecundity) and the absence of lethal factors in the male germ cells are hereditary.

C. G. L. W.

Rous, P. and **Larimore, L. D.** **The relation of the portal blood to liver maintenance.** *Proc. Soc. Exper. Biol. and Med.*, 1920, **17, 65.**

The occlusion of portal branches of the rabbit's liver leads ultimately to complete atrophy of the parenchyma of the deprived region and to hypertrophy elsewhere. Three-fourths of the liver may be reduced to a fibrous tag while the rest of the liver attains the bulk of the original organ. The atrophy is simple. It fails to progress when the bile-duct from the proliferating liver tissue is ligated and hypertrophy checked in this way. The fact that a parenchymal shift follows local changes in the portal stream has a bearing on the cause of alterations in the shape of the normal liver which have been attributed to pressure from the surrounding organs.

C. G. L. W.

Levy, R. L. and **Cullen, G. E.** **On the deterioration of crystalline strophanthin in aqueous solution.** *Proc. Soc. Exper. Biol. and Med.*, 1920, **17**, 63.

There is a rapid deterioration of solutions of strophanthin when these are sterilized in ordinary glass ampoules. The loss of strength is due to the action of the alkali dissolved from the glass. It is suggested that the solution should be made to contain a suitable buffer salt, e. g. acid potassium phosphate, which will control the change of reaction, or that the ampoules should be made of hard glass. C. G. L. W.

Eddy, W. H. and **Stevenson, H. C.** **The suitability of the 'Bachman test' for water-soluble B.** *Proc. Soc. Exper. Biol. and Med.*, 1920, **17**, 52.

The content of water-soluble vitamine B. may be ascertained by the gas production of yeast grown in Nägeli's solution containing glucose. It is claimed that the yeast test is more reliable than rat-feeding experiments. See Bachman, *Journ. Biol. Chem.*, 1919, **39**, 1919. C. G. L. W.

Hess, A. F. and **Unger, L. J.** **The rôle of fat-soluble vitamine in the dietary of infants.** *Proc. Soc. Exper. Biol. and Med.*, 1920, **17**, 49.

Infants varying in age from 5–12 months were given a diet deficient in fat-soluble vitamine consisting of 180 grm. of highly skimmed milk, 15–30 grm. of autolysed yeast, 15 c.c. of orange juice, 30 grm. of cotton-seed oil and cereal for older infants. The children did well for eight to nine months. The authors believe that either a very small amount of the vitamine is necessary or that feeding with a diet deficient in this accessory factor must be continued for a very long time to produce harmful results. They do not believe that rickets is brought about by the lack of this factor, especially as the disorder develops in children receiving large quantities of milk. Cod-liver oil is superior to cream or leafy vegetables in promoting growth.

C. G. L. W.

Macht, D. I. and **Mora, C. F.** **Effect of anaesthetization on the subsequent behaviour and intelligence of albino rats.** *Proc. Soc. Exper. Biol. & Med.*, 1920, **17**, 61.

Anaesthetization with nitrous oxide does not produce any change in the intelligence of the animals. Of the anaesthetics studied, chloroform was the most deleterious. A single administration of the drug for a few minutes was sufficient to impair the intelligence for that day. In cases where repeated anaesthesia was performed there was permanent loss of intelligence, and the animal had to be re-trained. C. G. L. W.

Partos, S. Bestimmung des durch Urease zersetzten Harnstoffs aus der CO_2-Komponente des Zersetzungsproduktes. [**Estimation of urea by urease, using the CO_2 component of the ammonium carbonate formed.**] *Biochem. Ztschr.*, 1920, **103**, 292.

The author has worked out a method of estimating urea, based upon the splitting of the urea with the enzyme urease. Instead of using the ammonia split off in the final estimation, he measures the volume of CO_2 evolved. R. A. P.

Schmidt, C. L. A. and **Allen, E. G.** **Further studies on the elimination of taurin administered to man.** *J. Biol. Chem.*, 1920, **42**, 55.

Certain authors have considered that taurin ($NH_2\ CH_2\ CH_2\ SO_3\ H$), the constituent of the taurocholic acid found in the bile, is excreted in the kidney in combination with urea. This is because they have found such a combination present in the urine. It was doubtful, however, whether this uramino-acid was not formed as a result of the method of treatment of the urine. The authors have used Van Slyke's method to settle the point. They found that the determinations of the neutral sulphur and amino-acid nitrogen in the urine of an individual, fed with taurin, agreed closely with the amount of taurin given. This indicates that taurin is not really excreted as taurocarbamic acid. The conclusion was further confirmed by showing that the administration of taurin in large doses was not followed by any alteration in the excretion of urea and ammonia. R. A. P.

Fenger, F. and **Hull, M.** **A study on the separation of the physiologically active portion of the posterior lobe of the pituitary body.** *J. Biol. Chem.*, 1920, **42**, 153.

One by one the substances of an internal secreting or hormone nature are being reduced to comparatively simple chemical bodies. It looks as if the pituitary will also give up its secret before long. These authors have shown that the active principle of the pituitary, which has a contractile action upon the uterus, seems to be linked in the fresh gland to a protein complex. When it is split off by treatment with hot 95 per cent. alcohol, the split product is amorphous in nature, hygroscopic, and very sensitive to desiccation. The ordinary crystalline bodies in the posterior lobe are apparently inorganic salts possessing no effect upon the uterus.

R. A. P.

Collip, J. B. 1. Osmotic pressure of serum and erythrocytes in various vertebrate types as determined by the cryoscopic method. 2. Effect of dilution on the osmotic pressure and the electrical conductivity of whole blood, blood serum, and corpuscles. 3. Osmotic pressure of tissues as determined by the cryoscopic method. 4. Maintenance of osmotic pressure within the nucleus. *J. Biol. Chem.*, 1920, **42**, 207.

The author, in confirmation of Macallum, has found that the nucleus of a cell is free from potassium, chlorine, phosphate, and carbonate-ions. The method used is a micro-chemical one. It is not claimed that his results are absolute, but, as such well-marked localizations of these various ions are found in other parts of the cell, it would appear that it can be believed that the nucleus is practically free from inorganic electrolytes. At present it has not been actually shown that sodium, calcium and magnesium are absent, but the absence of chlorine suggests that they cannot be present as inorganic electrolytes. If this reasoning is right, the osmotic pressure of the cell nucleus must be maintained by non-electrolytes or organic electrolytes such as dextrose, urea, or amino-acids. Determinations of the osmotic pressure of serum, blood corpuscles, and tissues by the cryoscopic method gave the following results. The osmotic pressure of blood corpuscles was less than that of the plasma in which they were suspended. The osmotic pressure of the tissues examined was, on the contrary, greater than that of the plasma The tissues investigated were pancreas, muscle, spleen, kidney, and heart. It would appear from this that the nucleus must have to maintain an osmotic balance of its own. The author is carrying on experiments to find out what actually happens in mitosis—whether electrolyte gets in among the chromosomes during the process. One feels that careful investigations of this nature may throw some light upon the mechanism of these intimate parts of the cell.

R. A. P.

Myers, C. N. and **Voegtlin, Carl. Chemical isolation of vitamines.** *J. Biol. Chem.*, 1920, **42**, 199.

Steenbock, H. and **Boutwell, P. W. Fat-soluble vitamine. VI. The extractibility of the fat-soluble vitamine from carrots, alfalfa, and yellow corn by fat solvents.** *J. Biol. Chem.*, 1920, **42**, 131.

Attempts to isolate the vitamines have been going on for some time. In 1897, Eijkman showed that rice polishings contain the antineuritic vitamine. which is dialysable and not precipitated from its solution by alcohol. Following Eijkman, Funk found that the substance which cures beri-beri is of a comparatively simple nature (it can be hydrolysed for some hours with 25 per cent. sulphuric acid without causing destruction of the vitamine). The active substance is precipitated with phosphotungstic acid and is mainly found in the silver nitrate-baryta fractions when subjected to silver precipitation. This fraction contains the histidin, pyrimidin, and nicotinic acid groups. Other workers, in a similar way, have been able to isolate vitamine products from various raw materials.

Myers and Voegtlin have worked for some time at the isolation of the antineuritic vitamine from brewers' yeast. They find incidentally that the vitamine can be extracted with fat. The active material can readily be extracted from dried yeast with acid methyl alcohol, and purified by the Funk method. By their method M. and V. have eliminated purins, histidin, proteins, and albumoses, leaving a liquid that can be crystallized and contains substances of the nature of histamin.

Steenbock and Boutwell have been trying to push our knowledge of the fat-soluble vitamine further. They find that alcohol and benzene are better solvents than fat for the fat-soluble vitamine of carrots and alfalfa. By treatment of the solution obtained, a fraction can be got containing the fat-soluble vitamine and the carotin (plant pigment) free from xanthophyll.

R. A. P.

Langworthy, C. F. and Deuel, H. J. Digestibility of raw corn, potato, and wheat starches. *J. Biol. Chem.*, 1920, **42**, 27.

Raw starches are generally believed to be practically indigestible. Fofanow found that raw wheat, oat, or rice starches were practically completely assimilated, whereas potato starch only in part. The authors have done some experiments upon this point. They made the starches used for the experiment into a kind of ice cream. In this condition it was not possible to obtain any evidence of rupture or swelling of the starch grains microscopically. Raw corn and wheat starches were shown to be completely assimilated. No trace of starch could be found in the faeces. Seven experiments upon raw potato starch gave digestibilities varying from 62–95 per cent. The eating of the potato starch was accompanied by a very excessive formation of gas and severe intestinal cramps.

R. A. P.

Hammett, F. S. Studies of variations in the chemical composition of human blood. *J. Biol. Chem.*, 1920, **41**, 599.

Much recent work has been directed to the study of the normal variations of individual constituents in the blood. With the exception of a complete account of the subject published by Gettler and Baker, one or more of the soluble nitrogenous constituents of the blood have been usually omitted. In order to obtain a complete set of such determinations for subsequent reference, the author has undertaken a set of estimations upon a series of nurses and hospital patients, in whom he could find no evidence of metabolic disorder. The estimations made were the following: the total nitrogen, non-protein nitrogen, urea nitrogen, creatinin nitrogen, creatin nitrogen, uric acid nitrogen, amino-acid nitrogen, rest nitrogen, and blood-sugar. Samples for analysis were taken three and a half hours after the first meal and not more often than once a week from the same individual. The individuals were not dieted because the amount of the uniform hospital diet used by an individual must be dependent ultimately upon the individual reaction to the food-stuffs eaten.

The results obtained are grouped under the following heads for discussion. Individual variability, group variability, influence of the time of withdrawal of the blood upon its composition and nitrogen distribution.

Individual variability. The composition of the blood varies from week to week in a given individual, but each analysed constituent tends to have its own degree of variation. The least variable constituent (as was to be expected) was shown to be the creatinin, after this, in order, total non-protein nitrogen, total nitrogen, creatin, sugar, uric acid, amino-acid, urea, and rest nitrogen. Some individuals are found to have greater variations in their constitutents from week to week than others. This is taken to represent differences in 'metabolic stability' between the individuals.

Group variability. Within the group of people dealt with, the following table represents the variations found:

	Range of Variation (mg.).	Average (mg.).	Average Duration %.	Relative Variability.
Creatinin N.	0·37– 0·60	0·47	7·3	100
Non-protein N.	27·3 –45·5	35·6	9·1	125
Total N.	2560–4290	307·0	9·4	129
Creatin N.	0·62– 1·78	1·31	11·5	158
Sugar	85–166	112·0	13·7	188
Uric acid N.	0·50– 1·16	0·78	14·9	204
Amino-acid N.	3·1 – 7·2	4·9	15·3	210
Urea N.	9·7 –25·1	17·1	16·6	227
Rest N.	3·7 –18·3	11·1	20·1	275

These figures are in fair agreement with those of other workers. They lead to the natural question as to why some constituents are so constant while others are so variable? The author thinks that 'the causes of these differences in variability cannot be attributed solely to differences in the amounts or nature of absorbed material since the order of variability tends to be the same in different individuals presumably ingesting quantitatively different diets'. The endogenous factor is apparently of considerable significance in the case of creatinin, and perhaps in that of uric acid, as Denis has recently found that the concentration of uric acid does not rise in the blood in normal individuals during the ingestion of purin-containing foods. The author regards the variability as a question of the metabolic mechanism specific for the species.

Influence of the time of withdrawal of the blood upon its composition. Gettler and Baker have stated that the concentration of the various blood constituents, whether taken before or after breakfast, falls within the normal limits. This is confirmed. There is evidence of a slightly lower metabolism before breakfast, as the non-protein nitrogen, the urea nitrogen, and the uric acid nitrogen are a little lower in amount. The sugar may be somewhat higher.

Nitrogen distribution in the blood. Changes in the level of the non-protein nitrogen tend to be accompanied by a change in the nitrogen distribution. The rest nitrogen tends to show the least change, whereas the urea tends to show the greatest diminution. Creatinin does not definitely change, and is therefore shown to be independent of the total non-protein nitrogen. The only specific relation brought out was that the rest nitrogen tended to increase in absolute amount as the urea nitrogen diminished.

Normal studies of this nature should form a good basis for the analysis of pathological conditions. At present the view seems to be held that it is the blood picture rather than the amount of any particular constituent that gives the clue to a pathological condition. R. A. P.

RADIOLOGY AND ELECTROLOGY

Radiotechnique

GUILLEMINOT. Sur un synchroniseur électrique permettant de fixer un radiogramme à une phase quelconque d'un tracé électrocardiographique ou sphygmographique. [**An electric synchronizer which enables one to fix a radiogram at a given phase of a cardiographic or sphygmographic tracing.**] *Bull. Soc. franç. d'électrothérap. et de radiol.*, 1919, July–Oct., 56. (*J. de radiol. et d'électrol.*, 1920, **4**, 37.)

The apparatus consists of: (1) A mechanical arrangement enabling one to obtain the release of X-rays at a given time after the signal furnished by cardiac pulsation. A spindle turns with a uniform movement and on it is mounted a wheel which, if free, is carried round with it because of a slight friction, but may be kept from revolving by a catch; the interrupter system of the X-ray circuit can be attached to the wheel at an angular distance from the catch and can be regulated at will. (2) An electrical arrangement enabling one to synchronize the start of the wheel with the selected moment of the cardiac cycle. A rubber armlet is placed on the fore-arm and is joined up with a Marey-reservoir tambour similar to that of Pachon's oscillometer and carrying a lever which oscillates at each systolic wave. This lever terminates in a copper wire which dips into a mercury junction at each pulsation, and thus closes the circuit of an electro-magnet which controls the catch immobilizing the wheel of the first-mentioned arrangement. The apparatus works as follows: arterial pulsation closes the circuit of the electro-magnet, and this, by displacement of the catch, releases the wheel. The wheel begins to revolve and, according to the arrangement adopted, completes the X-ray circuit, either immediately or $\frac{1}{10}$, $\frac{2}{10}$, $\frac{3}{10}$, &c., of the cardiac cycle later (the speed of rotation of the wheel being calculated so that 1 revolution = the duration of a cardiac cycle). The passage of the rays lasts $\frac{1}{10}$ of a second. If one has an apparatus powerful enough to obtain the image with this exposure, then the apparatus is stopped; but if one is obliged to renew the exposures, the apparatus is allowed to continue working, when each pulsation liberates the catch afresh, and a new passage of the rays is obtained at the identical phase of each succeeding heart's beat. In this way a cumulative effect is obtained. S. U. L.-B.

Radio-diagnosis

EVANS, W. A. Significance of annular shadows. *Am. J. Roentgenol.*, 1919, **6**, 510.

In discussing the differential diagnosis between a cavity in the lung and a localized pneumothorax, the author gives several aids. In the first place, the outline of a localized pneumothorax is irregular both as to contour and density, and it shades off gradually into the surrounding lung tissue, and practically all of the normal lung tissue structure can be seen throughout the area.

The pathology presented in other portions of the chest also helps; for instance, it would be unusual for a fibroid type of miliary tuberculosis to present a cavity, and it would be equally rare to find a cavity in peribronchial tuberculosis.

The most reliable method, however, is by serial plates. While the changes in cavity formation from week to week are relatively nil, the changes in a localized pneumothorax are quite marked even from week to week.

The clinical importance of air-pockets is that they are evidence of a progressive tuberculosis, for the lesion cannot develop unless there is ulceration and rupture of the lung tissue. R. W. A. S.

Ruggles, H. E. Calcification in angiomata. *Am. J. Roentgenol.*, 1919, **6**, 512.

This author draws attention to a form of calcification in angiomata which is apparently not well recognized. It appears in the form of multiple, small, cyst-like masses varying in diameter from a millimetre to a centimetre, or more, with a thin shell and an irregular mass in the centre, giving an appearance suggesting encysted parasites. These spots are scattered through the growth and probably represent calcified thrombi in the loops of the cavernous type of angioma.

The condition is apparently benign, and, as this type of growth may occur in the liver and intestine, it is possible that similar shadows may be found in these regions. R. W. A. S.

Laubry, Ch. et **Bordet, E.** Le cœur triangulaire; étude de radiologie clinique. [**The triangular heart; a study in clinical radiology.**] *Presse méd.*, 1919, No. 65, 633. (*Arch. d'électric. méd.*, 1919, **27**, 340.)

In certain radiological examinations the cardiac shadow assumes a triangular shape; the right and left sides correspond to the two oblique sides of a triangle; the base rests on the diaphragm; the apex, truncated, should be above the heart, on the mid-sternal line. The right edge is limited by a line from the base of the heart, directed straight downwards and outwards towards the diaphragm, which it touches, forming with it an obtuse angle open to the right. This feature constitutes one of the most important characteristics of the radiogram. The triangular image is pathognomonic of dilatation of the right ventricle. It is one of the indications that the myocardium has become involved in the course of affections normally attacking the right heart—pneumonia, emphysema, asthma, diseases of the left heart, and aortitis; in these cases radioscopy goes hand in hand with the clinical event, and is of great value in specifying the lesion and in showing its gravity. But this sign has a still greater importance when clinical facts are not sufficient to decide prognosis; observation of extra systoles, of cardiac instability, of tachycardia, are reported in cases where only the triangular heart enabled one to foresee the gravity of the condition. In the aged, in whom the right ventricle is early affected and early tends to react by dilatation, the triangular heart is the first sign of fatigue of the myocardium. Determination of its presence or absence, therefore, is of great importance and should it be present the case must be regarded as cardiac. S. U. L.-B.

Radio-therapy

Boije, O. A. Strålbehandling af myom och hemorragiska metropatier. [**Actinotherapy of myoma and haemorrhagic conditions of the uterus.**] *Finska läk-sällsk. handl.*, 1920, **62**, 1–28.

Boije's cases include 52 of myoma and 14 of various other haemorrhagic conditions of the uterus. In 41 out of 49 cases of myoma, X-ray treatment arrested the haemorrhage; in the other 8 cases it was reduced to normal but not wholly arrested. In 42 out of 44 cases examined after treatment the tumour was found to have shrunk much; in 9 cases its size had varied from that of a child's to that of a man's head. The reduction was so great in some cases that the tumour was barely demonstrable after treatment. In the remaining 3 cases the treatment was unsatisfactory, or reliable data were not available by which to judge of the effect of treatment. The period of observation was 4 to 5 years in 25 cases, 1 to 3 years in 13; the shortest observation period was 4 months. In 9 of the 14 cases of haemorrhage from the uterus, due to various causes, complete amenorrhoea was induced. In 4 cases normal menstruation was restored. No burns or other misfortunes followed this treatment.

Boije summarizes his experiences in the following 6 rules:

(1) Actino-therapy of myoma and haemorrhagic conditions of the uterus is undoubtedly superior to operative treatment in the presence of such complications as heart disease.

(2) Polypous, submucous, rapidly disintegrating and gangrenous myomata are not suited for actino-therapy, but require operative treatment.

(3) Pain, under certain conditions, is more rapidly and effectively relieved by operative treatment than by actino-therapy. If the former is temporarily contra-indicated by secondary anaemia or other complications rendering a general anaesthetic dangerous, it is advisable to control the haemorrhage by actino-therapy, and to defer operations till the anaemia has been relieved.

(4) Actino-therapy is contra-indicated in young women. The age limit should be 40 to 42 years. Treatment of a myoma under this age should be limited to a conservative operation, such as enucleation. In exceptional cases, however, menorrhagia and metrorrhagia in young women may be treated by carefully graduated actino-therapy.

(5) In women of 40 to 45 it is not advisable, from a psychological point of view, to attempt with massive dosage to suppress menstruation altogether. But there are exceptions to this rule.

(6) The selection of cases for actino-therapy must be critical and based on expert knowledge. With these reservations it may be claimed that, compared with operative treatment, actino-therapy achieves as much and is less dangerous.

Boije has found X-ray treatment is more effective when the dosage is massive and the treatment is intensive, than when the dosage is weak and the period of treatment is prolonged. He notes that Professor Forssell has come to the same conclusion with regard to the radium treatment of malignant disease of the uterus. With reference to the differential diagnosis of malignant and non-malignant disease of the uterus, Boije admits the following mistake. A patient was sent to him by a colleague for X-ray treatment, as heart disease and anaemia contra-indicated operative treatment. The upper limit of the tumour of the uterus reached the level of the umbilicus. Curiously enough, the tumour shrank so much under treatment with the X-rays that in barely 3 months it could no longer be detected by palpation above the symphysis. Her strength rapidly returned, and the anaemia became less marked. Some time after her return home symptoms arose which led to laparotomy by a local surgeon, who found malignant disease. The further course of this case is not recorded.

C. L.

Webster, J. H. D. **Roentgen-ray treatment of a case of early acromegaly.** *Arch. Radiol. & Electroth.*, 1920, **24**, 261.

Theoretically acromegaly should be eminently a disease amenable to X-ray treatment, especially in its early stages, when the anterior lobe of the pituitary would simply show a chromophil hyperplasia, and before secondary tumour-like formation, local pressure damage, and much skeletal change have been produced.

The author accordingly treated an early case of typical acromegaly by radiations. The effect was remarkable. The severe headache was rapidly relieved and soon entirely disappeared. The irritability and depression almost completely went. The weight decreased. The optic disks returned practically to the normal while the fields of vision greatly improved.

Unfortunately the patient was then lost sight of and eventually turned up again in a worse condition, when operative measures were taken.

R. W. A. S.

Mazérès, G. Sur le phénomène de Radiothérapie : lois qualitative et quantitative. [**Radio-therapeutic phenomena, qualitative and quantitative laws. Nomogram.**] *Arch. d'électric. méd.*, 1920, **449**, 40.

The author has collected the qualitative and quantitative laws of radiotherapy, derived from the results of Bergonié, Tribondeau, Bordier, and others, concluding the summary with a short account of the biochemical theory of Bordier. A synthesis of the three well-known laws of distance, filtration, and quantity in terms of time, styled the General Law of Quantitative Radio-therapy, is described, which allows one to obtain rapidly the required exposure. The duration of setting T, is found to be proportional to the square of the distance focus-skin H, to the quantity of radiation Q, required to fall on the region, and inversely proportional to the per cent. quantity transmitted, F, by the filter, all other things being equal, or $T = (\theta \times 100/q.h^2).\ H^2\, Q/F$ minutes where q is the quantity of radiation received at a distance h in time θ. A calibration of the X-ray tube is necessary, which can be made by one of the usual methods. The formula will remain true whatever may be the unit of radiation chosen. Dr. Mazérès describes a nomogram for calculating the value of T and demonstrates its use by working a typical example. For the same purpose a calculating slide rule, based on the logarithmic decomposition of the formula, has been constructed and a full description of it is given. L. H. C.

Radio-biology

Girard, P. Relation entre l'état électrique de la paroi de la cellule et sa perméabilité à un ion donné. [**Relation between the electrification of the wall of a cell and its permeability to a given ion.**] *Compt. rend. Acad. d. sc.*, 1919, **169**, 94 (*J. de radiol. et d'électrol.*, 1919, **3**, 526).

The state of polarization of a septum separating pure water from a solution of a dissociated salt makes the septum unequally permeable to the two ions of the salt. It is the same with the cellular wall when it is at a different potential from that of the medium. This difference of potential can be modified. Thus, red blood corpuscles in an isotonic neutral solution or serum carry negative charges. A certain concentration of the H-ions in the solution inverts this sign by fixing positive charges on the wall of the cell. In other ways the charges on the walls can be modified to greater or smaller extent on the negative or the positive side. The author has studied the chemical changes in red blood corpuscles subjected to various electrical conditions (of the wall). He comes to the conclusion that the sign and intensity of the charges have an obvious effect on these changes, particularly on the passage of Cl. *In vivo*, variations of the corpusular volume (for example, greater in venous than in arterial blood) must be due to these influences. S. U. L.-B.

Klein, G. und **Dürck, H.** Mikroskopische Befunde an Karzinomen nach Mesothorbestrahlung. [**Microscopic results in carcinoma treated with mesothorium.**] *Strahlentherapie*, **8**, 166. (*Zentralbl. f. Chir.*, 1919, **46**, 1005.)

The authors report on two tumours affected to a large extent by irradiation, in which the histological appearances were entirely different. (1) Inoperable squamous cell carcinoma of the face, which was healed. A bioscopic examination during the healing stage showed all transitional forms between round, typical epithelial nests and rope-like strands of flat compressed distorted cells. Widely different haematogenous cells of the 'leucocytoid' group occurred in the interstitial tissue, along with fibroblasts and endothelial proliferations. Deformed epithelial cells surrounded by phagocytic leucocytes were common. There is the picture of a reactive inflammation which must be regarded as a consequence of chemotaxis acting upon epithelial cells whose vitality has been profoundly damaged by the irradiation. (2) Colloid cancer of the caecum. A tumour the size of a man's head, which after irradiation became quite small. The growth ulcerated externally, led to a faecal fistula and death. Histologically, in the centre was unaltered typical colloid cancer. In the outer region were increased formation and sclerosis of connective tissue, which led to concentric strangulation of biological units of the new growth. All intermediate forms were found between unaltered alveoli filled with epithelial tumour cells and separate syncytial elements. The latter were nothing more than giant cells formed by cohesion of the remnants of alveoli after the vitality of their constituent cells had been heavily damaged by the irradiation.

S. U. L.-B.

Radium Technique

Laborde, S. Utilisation de l'émanation concentrée en appareils clos. [**Utilization of concentrated emanation in sealed tubes.**] *J. de radiol. et d'électrol.*, 1919, **3**, 501.

Whether the radium or emanation applicator is used one should note (*a*) the strength of the instrument, (*b*) the total energy expended during the application, (*c*) the duration of the latter. The strength of a radium applicator is usually defined by its 'charge' of radium, and that of an emanation tube can as well be expressed as the mean quantity of emanation it contains during an application. The power for both types can still be represented by the energy expended in unit time. In either instrument the energy expended during an application is proportional to the quantity of emanation, in millicuries, destroyed. With either applicator the dose will be determined by its duration and by the number of millicuries of emanation destroyed, in the case of the radium, and the mean millicuries in that of the emanation applicator, thereby rendering the notation equivalent for both cases.

The advantages of the radium applicator are, its simplicity, its constancy, and its economy of energy. Although emanation tubes are unsuitable for many research purposes, yet, from the therapeutic point of view, the regular diminution of their radiation may be unimportant if the idea is correct that heavy doses acting for a short time give better clinical results than small doses acting for a long time. The advantages of the emanation applicator are its cheapness and the ease with which the strength and dimensions of the instrument can be varied.

Concentrated radium emanation in sealed tubes has, up to the present, been used only by the physicist and by the larger hospitals, but organized distribution of emanation applicators is pending. The radiation emitted by them is the same, and produces the same biological effect as that emitted from radium applicators, but whereas the latter, in radio-active equilibrium, form sources of constant radiation the former are sources of temporary radiation diminishing exponentially to half value in 3·85 days. The emanation is extracted in vacuo from solutions of radium salts by the method of Mme Curie or that of Danne. With radium, either as salt or in solution, there is an inevitable consumption of energy, and the author discusses the most advantageous utilization of the radiation. There is least loss of energy when one uses tubes containing a radium salt, for when emanation tubes are used the energy is divided between the emanation and the parent radium solution and the amount of energy wasted is greater the longer the period between two extractions. This is demonstrated by a table giving, for different intervals between two extractions, the percentage quantity of radiation wasted. In practice, one allows usually 2, 4, or 8 days between each extraction, according to the amount of emanation required and the mass of parent radium. With radium tubes it is not possible to modify the energy once the tube is made, but with radium in solution one is able to divide up the emanation at will, but this method is accompanied by loss of energy. L. H. C.

Regaud, Cl. et **Ferroux, R.** Doses et durée d'application en radiumthérapie. Procédés de notation et de calcul ; table pour l'emploi de l'émanation du radium. [**Dosage and duration of application in radium therapy ; modes of notation and calculation ; table for use with radium emanation.**] *J. de radiol. et d'électrol.*, 1919, **3**, 481.

The authors discuss the problem of dosage and its notation together with the bases of the various modes of radiation measurement. With a tube containing radium in radio-active equilibrium the basis of evaluation of the total quantity of radiation may be either (*a*) the mgm.-hour of radium, (*b*) the millicurie hour of emanation, or (*c*) the quantity of emanation destroyed. The intensity of radiation is expressed, in (*a*) by the mass of radium, in (*b*) by the quantity of emanation present, and in (*c*) by the quantity of emanation destroyed in 1 hour. With a tube of emanation a difficulty arises due to the continuous and rapid decrease in its radiation, but the calculation of the mean quantity of emanation in the tube during an application, practically equal to the actual contents of the tube when half the time has elapsed, is simple. This quantity, expressed in millicurie-hours, corresponds to mgm.-hours of radium element, used when speaking of radium tubes. The most general and precise notation is that of millicuries destroyed during an application, and is equally applicable to the case of radium and to its emanation. A table simplifying the calculation of doses and the duration of application, based on the quantity of emanation destroyed, for use with emanation applicators is described. L. H. C.

Physiotherapy

McFee, W. D. Treatment of fibrous and cicatricial tissue by physical therapeutic methods. *Am. J. Electrotherap. & Radiol.*, 1919, **38**, 288.

In these papers, contributed to a general discussion by the American Electrotherapeutic Association, the previously known facts of the application of physiotherapy to conditions of fibrosis were described, with illustrations from individual experience, and with a general survey of the pathology and consequent therapeutic rationale.

Major McFee, having described the nature of cicatricial and fibrositic tissue, and of the conditions resulting, classified the remedial agencies available as heat, mechanical, and chemical action.

The first is applied by whirlpool or paraffin baths, lamps, diathermy and high frequency currents, the latter by various electrical methods, and the actinic radiations of ultra violet light, X-rays, and radium. The mechanical action is provided by vibration, massage, active exercise, and electrically provoked movements.

The massage and electrical methods are most usefully employed in combination with a preliminary use of heat in one or other form.

He lays stress on the importance of treating the primary pathological condition, as for instance in chronic fibrotic changes of joints, rather than attempting to alleviate the resulting local lesions alone. N. H. M. B.

Electrotherapy

Dubory. Du traitement de la névralgie du trijumeau par la galvanisation à haute intensité (Méthode du Prof. Bergonié). [**The treatment of trigeminal neuralgia by high intensity galvanization (Prof. Bergonié's method).** *Arch. d'électric. méd.*, 1920, **448**, 12.

Having described in detail the treatment and progress of two very severe and obstinate cases the author discusses the pathology of trigeminal neuralgia, and the history of its treatment by electrical methods. He considers that the most useful method is Bergonié's, propounded in 1897, the essential points of which are the following:

The electrode should cover the whole of the affected side of the face with perfect apposition and even pressure. To this end a mask electrode is cut out of thin tin and applied over moistened lint by means of three bands. The positive pole is used, and the dose is 35 to 50 ma. for 15 to 30 minutes or even an hour. It should be repeated daily for 20 to 30 days, and spaced out as the symptoms subside. A large negative electrode is applied to the back. Opinion is in favour of the positive rather than the negative as the active pole, but good results are claimed for either by some authors, as also for ionization. N. H. M. B.

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